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American Journal of Diseases of Children

VOLUME 47 APRIL, 1934 NUMBER 4

HYPOPHYSEAL INFANTILISM

TREATMENT WITH AN ANTERIOR HYPOPHYSEAL EXTRACT: PRELIMINARY STUDY

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NEW YORK

Webster defines a dwarf as "a diminutive human being"; Dorland, as "an abnormally undersized person." Turning to a definition of infantilism, one finds that it is "a condition in which the characters of childhood persist in adult life. It is marked by mental retardation, underdevelopment of the sexual organs and often, but not always, by dwarfness of stature." There follows a formidable classification.

In this article, we wish to discuss a type of arrested development presumably due to secretory deficiency of the anterior hypophysis. It is not mentioned by Dorland. With no claim to originality but because of the etiologic and descriptive significance of the term, we have chosen to call the condition hypophyseal infantilism. If one is to escape ambiguity, however, it had best be called dwarfism, since sufferers from this disorder are rarely mentally retarded. That they never become mentally mature, as regards the things which touch on or are influenced by sex, can be understood in the light of their asexual existence.

The physical make-up of this type, aside from stature, is essentially normal. Other than a relatively short lower measurement, a natural characteristic of early childhood, there is frequently a good symmetry of body. The patients are not obese, at least not excessively so. Some are quite thin. The genital apparatus remains in an undeveloped state, although probably not in excess of the soma. The secondary sex characters are markedly delayed or absent. If the condition is recognized early, the patients have the appearance of normal children, small for their age. Later a mature expression which is not compatible with their stature develops in many. As time passes this expression changes to a wizened, oldish look, more incongruous by contrast with their diminu-

Read before the Section on Pediatrics at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 15, 1933.

tive bodies. These facial characteristics are variable as to time of appearance, however, and may even be absent in early adult life.

In the differential diagnosis of hypophyseal infantilism one should eliminate, as nearly as possible, every other cause of arrested development. Unfortunately this is not always possible. The integrity of the germ plasm must be considered, as well as inherent statural deviations, the dietary and the physical condition of the patient. Considering all these factors and the interrelationship existing between many of them, it is doubtful whether any type of infantilism can be said to have an uncomplicated etiology. Occasionally, however, one is able to sift out the more common causative factors in arrested development with a reasonable degree of certainty and arrive at the diagnosis by exclusion. Patients with hypophyseal infantilism do not present gross evidence of dystrophy of the bones or joints so common to many types of dwarfism. Their parents and grandparents are usually of average height. Brothers and sisters reared in the same environment consistently outstrip them in the growth increment. Although the appetite is small, the diet has frequently been regulated with more than ordinary concern. Several of our patients have received a highly mineralized and vitaminized diet for a number of years. Chronic illness of a congenital, infectious, parasitic or metabolic nature may easily be, and of course should be, ruled out. There is nothing peculiar in the chemistry of the blood. More frequently than not, perhaps, one is able to demonstrate a tolerance for dextrose. The urine is grossly normal. The basal metabolic rate is moderately, although rather consistently, depressed. Roentgenologically, patients with this disorder present a normal or only slightly retarded bone age, unless the condition is severely complicated by hypothyroidism. The skeletal framework is smaller and more fragile than normal, and the epiphyses remain open much longer. If, in addition to the aforementioned picture, one is able to demonstrate pathologic changes in the bones in the region of the sella, more particularly a microsella or complete bridging of the clinoids, one is justified in assuming a relationship between the finding and retarded growth. Unfortunately when a proper technic is employed and an unbiased interpretation is placed on the result, such a finding is rare. While an apparently normal sella may argue against the diagnosis, the finding by no means excludes it. Smith and MacDowell [1] have recently shown that hereditarily dwarfed mice of the Dunn strain show a congenital absence of the acidophilic (growth-producing) elements in the hypophysis. It is therefore theoretically possible for a defective gene to account for the condition without producing

1. Smith, P. E., and MacDowell, E. C.: An Hereditary Anterior-Pituitary Deficiency in the Mouse, Anat. Rec. **46**:249, 1930; The Differential Effect of Hereditary Mouse Dwarfism on the Anterior-Pituitary Hormone, ibid. **50**:85, 1931.

changes in the sella. Cushing [2] also has shown that microscopic adenomas in the gland may produce profound alteration of the soma. One must also bear in mind the possibility of functional (neurocirculatory) disturbance without demonstrable antemortem pathologic changes. When all is said and done, however, the diagnosis must always remain in doubt except in the infrequent cases in which the hypophysis has actually been removed or is known to have been destroyed, or when postmortem examinations verify the diagnosis.

Space will not permit a résumé of the brilliant work on the anterior hypophyseal hormones leading up to the discoveries of Evans and Long.[3] In 1922, these observers discovered that intraperitoneal injections of fresh anterior hypophyseal substance into rats not only affects the estrus cycle, but also produces growth. Later Evans and his co-workers [4] were able to separate the growth-producing from the sex-influencing principle and test the former by using it on rats. Reichert,[5] using the growth-stimulating fraction intraperitoneally, stimulated growth in hypophysectomized puppies, and Putnam, Teel and Benedict,[6] by intraperitoneal injection of a similar, although entirely independent preparation, produced a condition simulating acromegaly in the dog. Cushing [7] and his co-workers have attempted to produce growth in a number of pituitary dwarfs by the intramuscular injection of potent extracts of the anterior lobe. The first preparation used (in a group of three dwarfs) quickly lost its growth-stimulating effect (tested on rats) while the second preparation, although retaining its potency, was discontinued after 110 days (used in one verified case). In no instance was Cushing certain of

2. Cushing, H.: The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestation (Pituitary Basophilism), Bull. Johns Hopkins Hosp. **50**:137, 1932.

3. Evans, H. M., and Long, J. A.: The Effect of the Anterior Lobe Administered Intraperitoneally upon Growth, Maturity and Oestrus Cycles of the Rat, Anat. Rec. **21**:62, 1921; Characteristic Effect upon Growth, Oestrus and Ovulation Induced by the Intraperitoneal Administration of Fresh Anterior Hypophyseal Substance, Proc. Nat. Acad. Sc. **8**:38, 1922.

4. Evans, H. M.; Cornish, R. E., and Simpson, M. E.: Potent, Sterile and Low Protein Extracts of the Growth Hormone from the Anterior Hypophysis, Proc. Soc. Exper. Biol. & Med. **27**:101, 1929. Evans, H. M., and Simpson, M. E.: Hormones of the Anterior Hypophysis, Am. J. Physiol. **98**:511, 1931.

5. Reichert, F. L.: Effects of Anterior-Pituitary Extract upon an Hypophysectomized Puppy, Proc. Soc. Exper. Biol. & Med. **27**:204, 1929.

6. Putnam, T. J.; Teel, H. M., and Benedict, E. B.: The Preparation of a Sterile Active Extract from Anterior Lobe of the Hypophysis, Am. J. Physiol. **84**: 157, 1928; Studies in Acromegaly: VIII. Experimental Canine Acromegaly Produced by Injection of Anterior Lobe Pituitary Extract, Arch. Surg. **18**:1708 (April) 1929.

7. Cushing, H.: "Dyspituitarism": Twenty Years Later; With Special Consideration of the Pituitary Adenomas, Arch. Int. Med. **51**:487 (April) 1933.

stimulating growth in height, although in the verified case an increase in weight and appetite and other subjective evidences of an effect were apparent.

In 1930, in conjunction with Dr. William Engelbach [8] we began treating a dwarfed girl, apparently suffering from hypophyseal infantilism, by intramuscular injections of a preparation of the anterior pituitary gland. This case was reported prematurely, and since there were so many discrepancies in the protocol, we think it advisable to correct these and to report the completed study after two years and six months of observation. The other five children included in this study have been added in the past two years. Four of them are suffering from arrested growth which we presume to be hypophyseal. The fifth is a girl who had a hypophysectomy at 10 years of age. Of the total of six, four have been given the growth-stimulating preparation for varying periods. One was treated by another method, and one was left untreated for twenty-three months and then given a growth-stimulating hormone. The last two serve as controls.

The preparation used is a semiturbid, aqueous, alkaline extract of the bovine anterior hypophysis, prepared by Evans and his co-workers.[9] The first batches were passed through a Seitz filter. Recent batches have not been thus filtered, but are preserved by the addition of merthiolate. All filtered material is cultured before use. It is kept frozen until a few hours before administration and injected into the gluteal muscles. Very little pain and no untoward reactions, aside from local irritation (with large doses), attended its use.

The conduct of the protocol has been as scrupulous as possible in problems of growth and development. Since there is a variation ranging from two-tenths to even five-tenths inch according to the time of day, the apparatus used, the technic employed and the peculiar idiosyncrasies of the examiner, all the measurements were made by one of us on a rigid wall standard by a special technic at the same hour of the day. The photographs were made against a black background marked off by 6 inch squares. The camera was locked in position and had a fixed focus. The illumination was the same in every case. The exposures were different owing to the variable tints of the skin. Every roentgenogram was taken by a roentgenologist with experience in cranial roentgenography. A critical, unbiased interpretation was placed on the result.

In order to avoid repetition, the negative findings in these children, with a few exceptions, will be considered en masse. In no instance was either parent under 60 inches in height. In four instances, both parents

8. Engelbach, W.: The Growth Hormone, Endocrinology **16:** (Jan.-Feb.) 1932.

9. From the Department of Biological Research, University of California, Berkeley.

were over 66 inches. There is no history of dwarfism in any of the families. Physical examination revealed nothing abnormal in the heart, lungs or abdomen of any of the patients. The urine was normal in all. What examinations of feces were made gave negative results for intestinal nematodes. All the patients had negative Wassermann reactions.

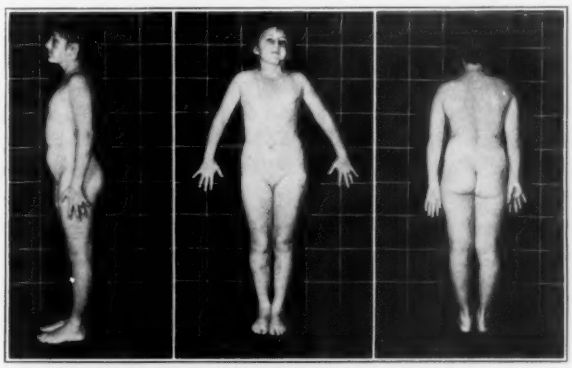

Fig. 1 (case 1).—Development of patient at about 12 years of age.

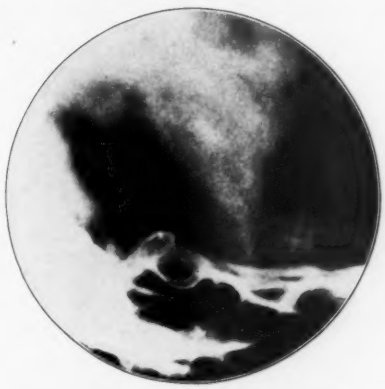

Fig. 2 (case 1).—Roentgenogram showing microsella, with approximation of clinoid processes.

The blood picture was normal for all except two, who presented a mild secondary anemia. All other physical and laboratory observations will be discussed individually.

REPORT OF CASES

CASE 1.—*History.*—B. P., a girl, aged 12 years and 1 month, of Anglo-Saxon descent, complained of retarded growth. The condition had been suspected at 9 years. The annual increment in the previous four years was 1.1 inches. (The average normal annual increment for the same period is 2.2 inches.) The per-

sonal history was essentially unimportant; the diet was apparently adequate and well balanced.

The family history revealed no abnormalities; the father's height was 72 inches; the mother's, 60.5 inches. A brother, aged 16 years, was 69 inches in height. The patient had no sisters.

Examination.—The general examination showed coxa vara, lumbar lordosis and an infantile configuration.

Psychologic: The patient had an intelligence quotient of 130, and showed excellent comprehension and concentration; the reactions were immature.

Laboratory: The tests showed an average basal metabolic rate of —10.6 per cent for four readings on different days. The hemoglobin was 68 per cent (Sahli); the sugar tolerance was high.

Roentgenographic: The wrist corresponded to that of a child aged 11 years. A microsella with approximation of the clinoid processes was seen.

Measurements: The height was 51 inches (approximately 6.6 inches under the average for the patient's age). The upper measurement was 27.9 inches; the lower,

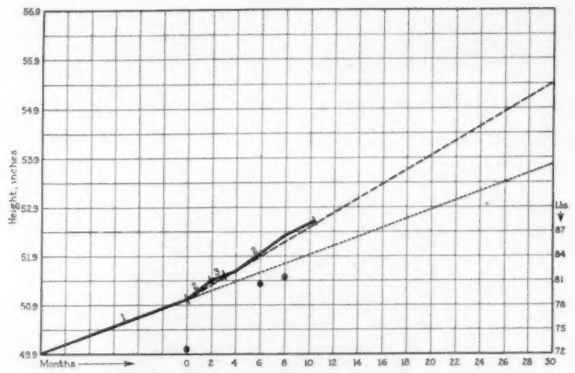

Fig. 3 (case 1).—Actual increment as compared with the estimated and average normal. The solid line represents the actual growth: *1*, during the year prior to observation; *2*, during the administration of the growth-stimulating hormone; *3*, during interruptions in the treatment. The dotted line represents the estimated growth on the basis of the average for the preceding four years. The dash line shows the average normal growth increment for girls from 12 to 15 years of age. The large dots represent the weight.

23.1 inches. The weight was 72.5 pounds ([32.87 Kg.], approximately 13.7 pounds [6.21 Kg.] overweight for the height).

Previous Treatment.—The patient had received a thyroid preparation and an anterior lobe pituitary preparation for varying periods.

Observation.—A period of observation and treatment was started on June 13, 1932. The alkaline extract of the bovine anterior hypophysis was given five days each week, intragluteally. The maximum daily dose was 7 cc. The present observation ended on May 1, 1933, the period of observation having extended over ten and one-half months. The total amount of hormone administered was 600 cc.; the actual increment, 1.6 inches. The estimated increment for ten and one-half months, based on the average for the previous four years, was 0.96 inches. The

average normal increment for the same age is 1.55 inches. The gain in weight for the period of observation was 9 pounds (4.08 Kg.).

CASE 2.—*History.*—W. A., a girl, aged 14 years and 9 months, of Anglo-Saxon parentage, complained of retarded growth, retarded development, headaches and poor vision. The retarded growth followed curettement of the pituitary area. The annual increment for the previous four years was 1 inch. (The average normal

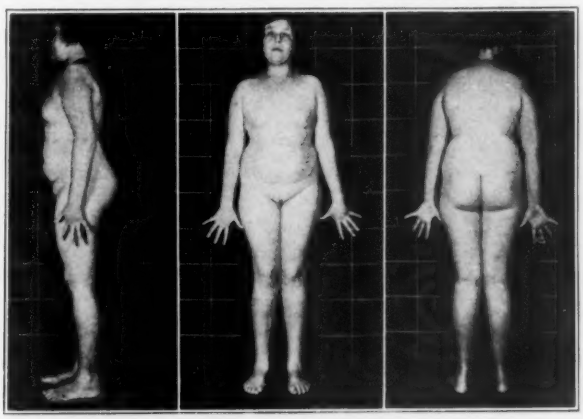

Fig. 4 (case 2).—Appearance of hypophysectomized patient.

Fig. 5 (case 2).—Roentgenogram of sella area showing operative defect and calcification in hypothalamic region.

annual increment for the same period is 2 inches.) The personal history was essentially unimportant until the age of 9 years, when symptoms of tumor of the brain appeared. Two craniotomies revealed a large suprasellar cyst. The pituitary area was curetted on May 7, 1926. The family history revealed no abnormalities. The father was 67 inches in height; the mother, 67.3 inches; a sister, 64 inches.

Examination.—The general examination disclosed moderate obesity, absence of secondary sex characters and contracted visual fields.

Psychologic: The patient had an intelligence quotient of 87, with fair comprehension and fair concentration. Her reactions were very immature and her behavior abnormal.

Laboratory: Four readings on different days showed an average basal metabolic rate of —11.0 per cent. The hemoglobin was 80 per cent (Sahli); the sugar tolerance was high, with low renal threshold.

Roentgenographic: The wrist corresponded to that of a child between 13 and 14 years of age. There was nonclosure of metacarpal and phalangeal epiphyses. The sella showed a large defect in the parietal region with almost complete bony regeneration throughout the operative defect. The normal contour of the sella was entirely lacking. Both the anterior and the posterior clinoids had been removed. The floor of the sella was smooth and firm. There was no evidence of destruction or erosion.

Measurements.—The height was 56.2 inches (approximately 6.1 inches under the average for the patient's age). The upper measurement was 28.4 inches; the lower, 27.8 inches. The weight was 94 pounds ([42.64 Kg.], approximately 18.8 pounds [8.53 Kg.] overweight for the height).

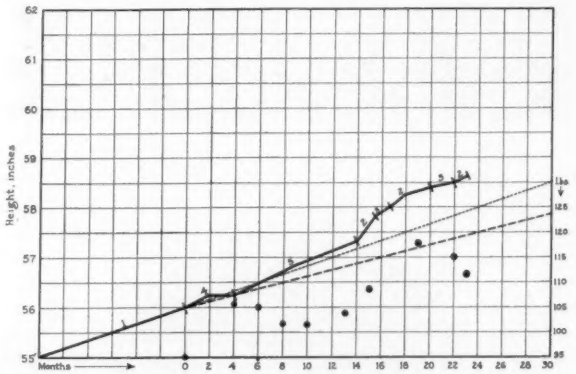

Fig. 6 (case 2).—Actual increment as compared with the estimated and average normal. The solid line represents the actual growth: *1*, during the year prior to observation; *2*, during administration of the growth-stimulating hormone; *3*, during interruptions in the treatment; *4*, during anterior lobe pituitary and extract of posterior lobe pituitary therapy; *5*, during the administration of a prolan from the urine of pregnant women. The dotted line represents the estimated growth on the basis of the average for the preceding four years; the dash line, the average normal growth increment for girls from 15 to 17 years of age. The large dots represent the weight.

Previous Treatment.—The patient had received no previous treatment.

Observation.—Observation was begun and treatment started on March 11, 1931. An anterior lobe pituitary preparation and solution of pituitary were administered in doses of 1 cc. each five days a week. Observation ended on July 11, 1931. The actual increment was 0.2 inch. The estimated increment for four months, based on the previous average for four years, was 0.3 inch. The normal average for the patient's age is 0.2 inch. A second period of observation and treatment was begun on July 11, 1931. Prolan from the urine of pregnant women was given in doses of 1 cc. five times a week. The period of observation ended on May 8, 1932, the patient having been under observation for ten months. The total amount of the

preparation administered was 190 cc. The actual increment in ten months was 1.1 inches. The estimated increment for ten months, based on the previous average for four years, was 1 inch. The normal average for that age is 0.7 inch. The third period of observation and treatment was begun on May 19, 1932. An alkaline extract of the bovine anterior hypophysis was given five days a week, intragluteally. The maximum daily dose was 4 cc. The observation ended on Feb. 19, 1933. The total amount of hormone administered was 535 cc. The actual increment in nine months was 1.4 inches. The estimated increment for nine months,

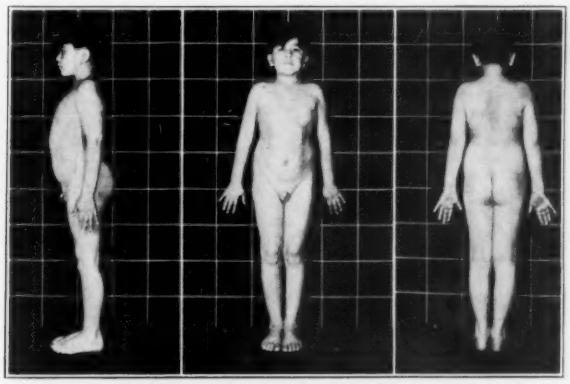

Fig. 7 (case 3).—Appearance of patient at about 13 years of age.

Fig. 8 (case 3).—Shallow sella with rudimentary anterior clinoids and no posterior clinoids.

based on the average for the previous four years, was 1 inch. The normal average for that age is 0.55 inch. The gain in weight for the period of observation was 17 pounds (7.71 Kg.).

CASE 3.—*History.*—V. M., a boy, aged 13 years and 2 months, of Spanish-American parentage, complained of retarded growth and genital hypoplasia. The condition had been suspected at 9 years. The annual increment in the previous four years was 1.1 inches. (The average normal annual increment for the same period is 2.1 inches.) The personal history was essentially unimportant. The diet was apparently adequate and well balanced.

The family history revealed no abnormalities. The father's height was 66 inches; his weight, 148 pounds (67.12 Kg.); the mother's height was 62 inches, her weight, 115 pounds (52.16 Kg.). Four brothers and two sisters were of average stature.

Examination.—The general examination showed lumbar lordosis, genital hypoplasia, left cryptorchidism and an infantile configuration.

Psychologic: The patient's intelligence quotient was 85. Comprehension and concentration were poor. The reactions were very immature.

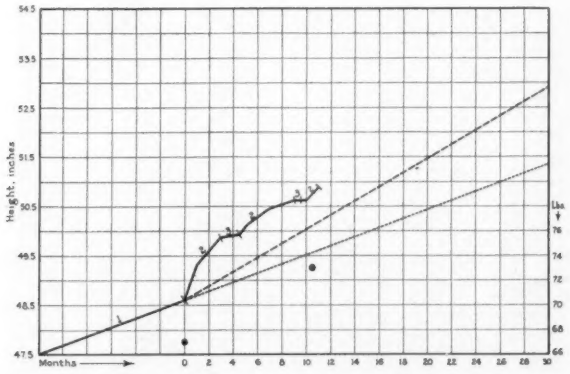

Fig. 9 (case 3).—Actual increment as compared with the estimated and average normal. The solid line represents the actual growth: *1*, during the year prior to observation; *2*, during the administration of the growth-stimulating hormone; *3*, during interruptions in the treatment. The dotted line shows the estimated growth on the basis of the average during the preceding four years. The dash line shows the average normal growth increment for boys from 13 to 15 years of age. The large dots represent the weight.

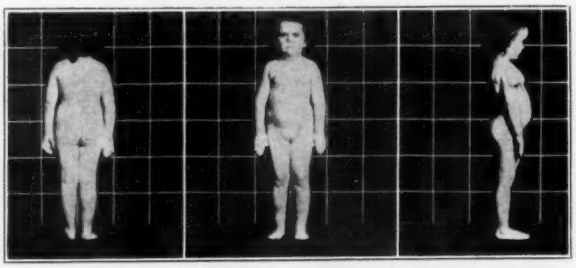

Fig. 10 (case 4).—Retarded growth of patient, aged 9 years and 8 months.

Laboratory: Four readings on different days showed an average basal metabolic rate of —16.0 per cent. The hemoglobin was 78 per cent (Sahli). The sugar tolerance was high.

Roentgenographic: The wrist corresponded to that of a child aged 9 years. The sella showed a very shallow cavity. The anterior clinoids were rudimentary. There were no posterior clinoids.

Measurements: The height was 48.5 inches (approximately 10.4 inches under the average for the patient's age). The upper measurement was 25.9 inches. The

lower, 22.4 inches. The weight was 67 pounds ([30.39 Kg.], approximately 15.4 pounds [6.98 Kg.] overweight for the height).

Previous Treatment.—No previous treatment had been given.

Observation.—Observation was begun and treatment started on May 28, 1932. An alkaline extract of the bovine anterior hypophysis was administered five days a week, intragluteally. The maximum daily dose was 6 cc. The present observation ended on May 1, 1933. The patient was under observation for eleven months. The total amount of hormone administered was 380 cc. The actual increment was 2.4 inches. The estimated increment for eleven months, based on the average for the previous four years, was 1 inch. The average normal increment for the corresponding age is 1.65 inch. The weight gained during the period was 6 pounds (2.72 Kg.).

CASE 4.—*History.*—J. M., a girl, aged 9 years and 8 months, of Anglo-Saxon parentage, complained of retarded growth. The condition had been suspected at 3 years. The annual increment for the previous four years was 1 inch. (The average normal annual increment for the same period is 2.1 inches.) The personal

Fig. 11 (case 4).—Normal appearance of sella.

history was essentially negative. The diet was apparently adequate and well balanced.

The family history disclosed no abnormalities. The father's height was 68.5 inches; the mother's, 60 inches. There were no sisters or brothers.

Examination.—The general examination showed genu valgum, lumbar lordosis, a wizened expression, an infantile configuration, thin scanty hair and wrinkled skin.

Psychologic: The intelligence quotient was 106. Comprehension and concentration were excellent; the reactions were immature.

Laboratory: Four readings on different days showed an average basal metabolic rate of —4.0 per cent. The hemoglobin was 66.5 per cent (Sahli). The sugar tolerance was high.

Roentgenographic: The wrist corresponded to that of a child aged 8 years. The sella was normal in appearance.

Measurements: The height was 35.2 inches (approximately 16.7 inches under the average for the patient's age). The upper measurement was 19.2 inches, the lower, 16 inches. The weight was 27.5 pounds ([12.47 Kg.], approximately 1.5 pounds [0.68 Kg.] underweight for the height).

Previous Treatment.—No previous treatment had been given.

Observation.—A period of observation was begun and treatment started on Nov. 13, 1930. An alkaline extract of the bovine anterior hypophysis was administered five days a week, intragluteally. The maximum daily dose was 12 cc. The

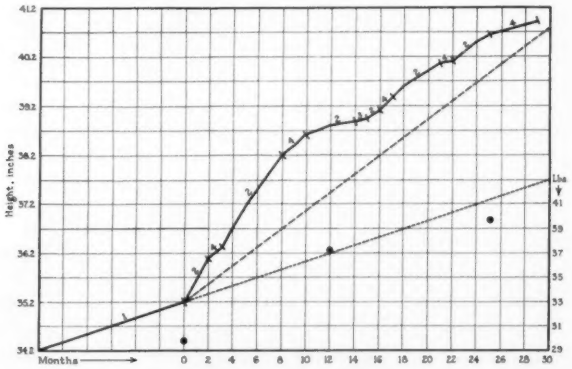

Fig. 12 (case 4).—Actual increment as compared with the estimated and average normal. The solid line indicates the actual growth: *1,* during the year prior to observation; *2,* during the administration of the growth-stimulating hormone; *3,* during the administration of calcium lactate, thyroid, and haliver oil; *4,* during interruption in the treatment. The dotted line represents the estimated growth on the basis of the average during the four preceding years. The dash line shows the average normal growth for girls from 9 to 12 years of age

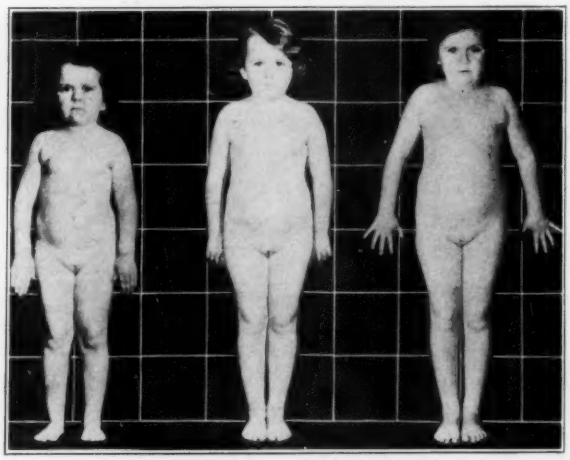

Fig. 13 (case 4).—Comparison of height, facial expression and configuration at beginning of treatment, nine months later and two years later.

treatment was discontinued on Dec. 23, 1932. The patient was under observation for twenty-five months. The total amount of hormone administered was 2,539 cc. The actual increment was 5.4 inches; the estimated increment for twenty-five months, based on the average for the previous four years, was 2.29 inches. The

average normal increment for that age is 4.6 inches. During the period from Dec. 23, 1932, to April 23, 1933, no treatment was given. The increment was 0.3 inch; for the previous four months it was 0.6 inch. The weight gained during that period was 10 pounds (4.53 Kg.).

There was a definite change in the appearance and configuration of this child. From a wizened, oldish expression, her appearance became more like that of a normal child. The knees apparently became straighter, the hair more glossy and luxuriant, and the skin more pliable and warm.

CASE 5.—*History.*—M. W., a girl, aged 10 years and 10 months, of Spanish-American parentage, was observed as a control. There was retarded growth. The condition had been suspected at 8 years. The annual increment for the previous four years was 1.1 inches. (The average normal annual increment for the same period is 2.1 inches.)

The patient had had an appendectomy at the age of 7 years. Otherwise the personal history was essentially unimportant. The diet was apparently adequate and well balanced.

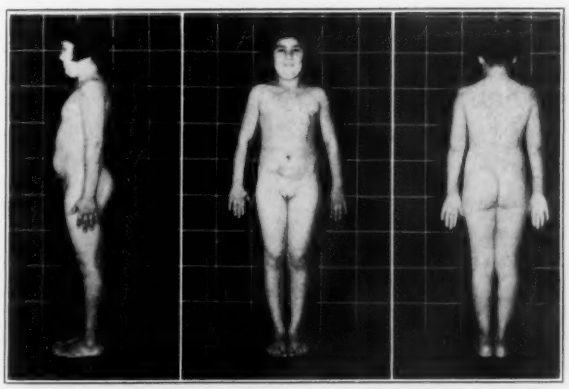

Fig. 14 (case 5).—Patient at age of 10 years and 10 months, observed as a control.

The family history revealed no abnormalities. The father's height was 64 inches; his weight, 150 pounds (67.04 Kg.). The mother's height was 62 inches, and her weight, 152 pounds (68.94 Kg.). Two brothers and two sisters were of average normal stature.

Examination.—The examination revealed moderate obesity and an infantile configuration.

Psychologic: Psychologic examination showed an intelligence quotient of 81, fair concentration, poor comprehension and very immature reactions.

Laboratory: Four readings on different days showed an average basal metabolic rate of —11.0 per cent. The hemoglobin was 76 per cent (Sahli). The sugar tolerance was high.

Roentgenographic: The wrist corresponded to that of a child aged 10 years. The sella was normal in appearance.

Measurement: The height was 49.1 inches (approximately 6 inches under the average for the patient's age). The upper measurement was 26 inches; the lower, 23.1 inches. The weight was 66.5 pounds ([30.16 Kg.], approximately 14.5 pounds [6.47 Kg.] overweight for the height).

Previous Treatment.—The patient had received no previous treatment.

Observation.—Observation and treatment were started on Dec. 23, 1930. One grain (0.06 Gm.) of desiccated thyroid gland with high iodine content with 10 grains (0.65 Gm.) of desiccated whole pituitary gland was given orally each day. Observation ended on March 18, 1932. The actual increment in fifteen months was 1.6 inches. The estimated increment for fifteen months, based on the average for

Fig. 15 (case 5).—Normal appearance of sella.

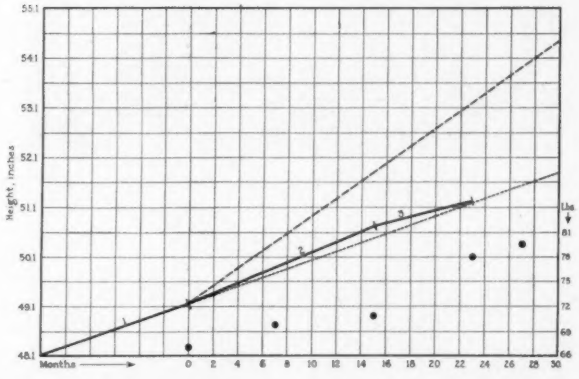

Fig. 16 (case 5, control).—Actual increment as compared with estimated and average normal. The solid line represents actual growth: *1,* during year prior to observation; *2,* during the administration of desiccated whole pituitary gland (10 grains daily) and desiccated whole thyroid gland (1 grain daily); *3,* during the intramuscular administration of 1 cc. of an anterior lobe pituitary preparation three times each week. The dotted line represents the estimated growth based on the average for the previous four years. The dash line shows the average normal increment for girls from 11 to 13½ years of age. The large dots represent the weight.

the previous four years, was 1.25 inches. The average normal increment for that age is 2.6 inches. The second period of observation and treatment was begun on

March 18, 1932. An anterior lobe pituitary preparation was given intramuscularly three days a week in doses of 1 cc. The period of observation ended on Nov. 15, 1932. The child had been under observation for eight months. The total amount of anterior lobe pituitary preparation administered was 105 cc. The actual increment was 0.5 inch. The estimated increment for eight months, based on the average for the previous four years, was 0.7 inch. The average normal increment for that age is 1.4 inches. The weight gained during the period of observation was 11 pounds (4.98 Kg.).

CASE 6.—*History.*—F. O., a boy, aged 11 years and 5 months, of Spanish-American parentage, was observed as a control. There was retarded growth; the condition had been suspected at 8 or 9 years. The annual increment in the previous four years was 1.4 inches. (The average normal annual increment for the same period is 2 inches.) The personal history was essentially unimportant. The diet was apparently adequate and well balanced.

The family history disclosed no abnormalities. The father's height was 65 inches; his weight, 140 pounds (63.50 Kg.). The mother's height was 65 inches;

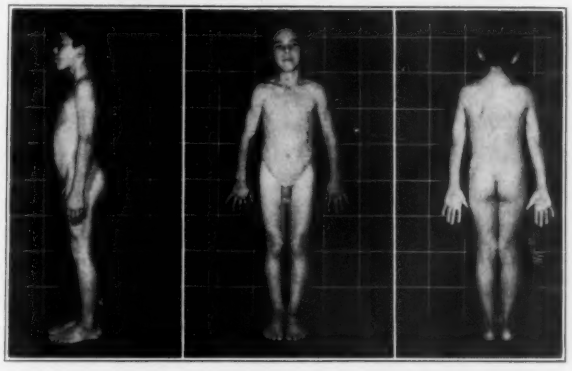

Fig. 17 (case 6).—Retarded growth of boy, aged 11 years and 5 months, observed as a control.

her weight, 138 pounds (62.58 Kg.). Five brothers and one sister were of average stature. One sister, aged 8 years, was 3 inches under the average stature for her age.

Examination.—The following conditions were noted: lumbar lordosis, moderate genital hypoplasia and an infantile configuration.

Psychologic: The patient had an intelligence quotient of 98. Comprehension and concentration were fair; the reactions were immature.

Laboratory: Tests revealed an average basal metabolic rate of + 12.0 per cent for two readings on different days. The hemoglobin was 80 per cent (Sahli). The sugar tolerance was normal.

Roentgenographic: The wrist corresponded to that of a child aged 11 years. The sella was normal in appearance.

Measurements: The height was 47 inches (approximately 9.2 inches under the average for the patient's age). The upper measurement was 26.5 inches; the lower, 20.5 inches. The weight was 51.8 pounds ([23.49 Kg.], approximately 10.7 pounds [4.85 Kg.] overweight for the height).

Previous Treatment.—The patient had received no previous treatment.

Observation.—Observation was begun on Feb. 28, 1931, and ended on Feb. 4, 1933. This child, being observed as a control, received no treatment. The actual increment in twenty-three months was 2.7 inches. The estimated increment for twenty-three months, based on the average for the previous four years, was 2.68 inches. The average normal increment for that age is 3.7 inches. A second period of observation was begun and treatment was started on Feb. 4, 1933. An alkaline extract of the bovine anterior hypophysis was administered five days a week, intra-

Fig. 18 (case 6).—Sella showing rudimentary anterior clinoids and large posterior clinoids.

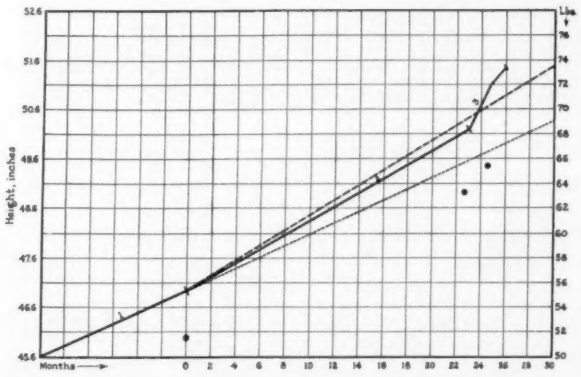

Fig. 19 (case 6).—Actual increment as compared with the estimated and average normal. The solid line represents the actual growth: *1,* during the year previous to observation; *2,* during a twenty-three month period of observation when no treatment was given; *3,* during the administration of the growth-stimulating hormone. The dotted line represents the estimated growth based on the average for the previous four years. The dash line shows the average normal increment for boys from 11 to 14 years of age. The large dots represent the weight.

gluteally. The maximum daily dose was 6 cc. The present observation ended on May 1, 1933. The child was under treatment for three months. The total amount of hormone administered was 180 cc. The actual increment was 1.2 inches. The

estimated increment for three months, based on the average for the previous four years, was 0.45 inch. The average normal increment for the same age is 0.45 inch. The weight gained during that period was 14 pounds (63.5 Kg.).

SUMMARY

Six children, presumed to have a secretory deficiency of the anterior hypophysis (verified in one), have been studied for over two years. Four were treated by the intragluteal injection of a growth-stimulating fraction of the bovine anterior hypophysis. One was treated by another method. One was left untreated for twenty-three months and then given the growth-stimulating fraction. The last two patients served as controls. The growth increment of the four treated patients was considerably in excess of the expectancy, as computed from the average for the previous four years, and slightly in excess of the theoretical normal for their ages. It was not definitely determined whether the rate was in direct ratio to the amount of substance administered, or whether there was a difference in the potency of the filtered material (without a preservative) and the filtered material (with merthiolate). Our belief is that the increment was more rapid in the first few months of treatment than subsequently. If true, this may have been due either to a difference in the physiologic response or to the difference in material. One child who received treatment changed in configuration and appearance. The growth increment for the two control cases was slightly in excess of the expectancy, but below the theoretical normal. The increment for the control case, in which the growth-stimulating fraction was given later, was in excess of the theoretical normal and several times the previous rate. However encouraging the results have been, we do not think that stimulation of growth has been proved, except in a single instance. A year or more of close observation is necessary to verify the findings in the others.

CONCLUSIONS

From these observations, it appears that:

1. Growth has been stimulated in children by the intragluteal administration of a growth-stimulating fraction of the anterior hypophysis.

2. The substance produced changes in the facial expression and configuration of a dwarfed child.

3. In its present potency and by this method of administration, the preparation will not rehabilitate one who has fallen far behind in development, unless, perhaps, it is given in massive doses and over a prolonged period.

4. Even in its present potency, the preparation, if administered early in the proper dose and over a sufficient period, may be of clinical value in certain cases of mildly arrested development and in the prevention of hypophyseal infantilism.

ABSTRACT OF DISCUSSION

DR. J. VICTOR GREENBAUM, Cincinnati: To influence growth in children who are undersized owing to hypopituitary conditions is of great importance to the general practitioner who is frequently urged by parents to do something.

In my opinion, Dr. Shelton has been unduly conservative in his conclusions. The charts reveal that these children showed definite growth. They all grew faster with treatment than without it.

It is interesting that in his case he did not differentiate, as we did, between the Lorrain-Levy type of condition, in which the secretion of the anterior lobe only is deficient, and the typical Fröhlich type or dystrophia adiposogenitalis, in which the secretion of the posterior lobe also is deficient. In the latter type the patient is particularly fat and shows the girdle distribution of fat.

We have continued to treat our twelve patients in these two groups for the past year and have continued to secure satisfactory growth. In one case the growth has come up to the normal. In addition, we have a number of control cases in which the parents refused treatment, and in these patients growth is by no means as rapid as in the treated patients.

Dr. Shelton has also emphasized the necessity of persistent treatment. This is of paramount importance. Intermittent and sporadic treatment will not give good results. He also mentioned other factors involved with endocrinopathies that must be considered.

Dr. Cheche Wang, of Cincinnati, reported in the May issue of the *Journal of Biologic Chemistry* a case of Lorrain-Levy infantilism, on which she made some detailed metabolic studies for fifty-one days. The child was given a normal diet, without any medication. During this period of observation the patient showed a tremendous rate of growth, in fact two hundred times the growth expectancy. When the child was discharged, returned to its home environment and again received its usual diet, this acceleration of growth ceased.

I feel that the best results can be obtained with endocrine therapy by persistently using the material available at present, although I am delighted to know that a more potent preparation, such as the growth-stimulating hormone extracted from the bovine anterior hypophysis, will soon be available.

DR. E. KOST SHELTON, Santa Barbara, Calif.: We did not attempt to differentiate between the simple anterior pituitary deficiency and the so-called bilobar disorder because we are not at all convinced that Fröhlich's disease is simply bilobar. There is considerable contention as to the etiology of this disorder. We have dealt only with the so-called Lorrain-Levy type of hypophyseal infantilism and have attempted to control our cases in such a manner so as to either prove or disprove the efficacy of the treatment employed.

Other forms of treatment may have been indicated in a number of our patients. In fact, after the initial experimental period of medication with the growth-stimulating hormone alone, a few were given small doses of thyroid and a diet high in calcium and vitamins. I believe that the most promising regimen for children with this and like deficiencies is a diet high in minerals and in vitamins, a good environment and the endocrine substitution indicated.

From a careful study, we believe that hypothyroidism is not an essential feature of this group. No patient presented marked retardation of carpal development, which is a more or less consistent finding in dwarfs suffering with severe hypothyroidism. Children with hypothyroidism frequently gain rapidly on thyroid substitution alone. One such patient in our group gained 4.7 inches within a year without other forms of treatment. The choice of an intelligent therapeutic regimen, therefore, depends much on the differential diagnosis.

ELECTROCARDIOGRAPHIC STUDIES DURING PNEUMONIA IN INFANTS AND IN CHILDREN

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AND
M. I. VINNECOUR, M.D.
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Comprehensive electrocardiographic studies have been made on large groups of normal infants and children since the first observations recorded by Funaro.[1] Recently, similar normal observations have been established for premature infants.[2] A considerable number of studies, recording changes in the electrocardiogram, have been reported for infants and children suffering from rheumatic infections,[3] diphtheria[4]

From the Sarah Morris Hospital for Children, and the Heart Station, Michael Reese Hospital.

Aided by the Emil and Fanny Wedeles Fund for the Study of Diseases of the Heart and Circulation.

Read before the Section on Pediatrics of the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 16, 1933.

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2. Londe, S.: Some Aspects of the Circulation in the Premature Infant, Am. J. Dis. Child. **44**:110 (July) 1932.

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4. (*a*) Butler, S., and Levine, S. A.: Diphtheria as a Cause of Late Heart-Block, Am. Heart J. **5**:592 (June) 1930. (*b*) Reid, W. D.: Permanent Bradycardia Following Diphtheria, ibid. **5**:524 (April) 1930. (*c*) Marvin, H. M.: The Effect of Diphtheria on the Cardiovascular System: I. The Heart in Faucial

(*Footnote continued on next page*)

and scarlet fever.[5] So far as we can ascertain, no serial electrocardiographic studies have been made during pneumonia in infants and children.

This article consists of reports on a series of electrocardiograms taken on individual infants and children during the course of pneumonia. As many tracings as possible were made on successive days during the acute illness, and a control tracing was taken on each patient some time after complete recovery. By comparing the control record with the tracings taken during the height of the illness, the changes in the electrocardiogram during the acute stage could be accurately determined. All the infants and children examined in this study were suffering from bronchopneumonia. None received digitalis, atropine or any drug which might act on cardiac conduction or cardiac muscle. The ages of our patients ranged from 4 months to 7 years. Altogether, thirty-eight electrocardiograms were made on eight individual patients.

Only one serial study has been made on the electrocardiographic changes during pneumonia in adults.[6]

REPORT OF CASES

CASE 1.—R. E., a boy, aged 4 months, was admitted to the hospital on April 4, 1932, and discharged on April 22. There was a history of cough and difficult breathing for four days and fever for two days, accompanied by irritability. At admission the patient was well developed, well nourished and acutely ill. The lungs showed no impairment of resonance. There were numerous dry and moist râles over both lungs, especially at the bases. The heart borders were within normal limits, and there was no cardiac displacement. The cardiac rate was very

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rapid; the tones were clear, and no murmurs were heard. The abdomen was distended but was not rigid.

On April 6 the temperature was 100 F. by rectum; respirations were rapid. Marked dyspnea and paroxysmal cough were present. There was considerable abdominal distention. The following day the temperature became normal and remained so. Thereafter the râles gradually disappeared, and recovery was uneventful.

An electrocardiogram was taken on April 6, while the patient was acutely ill. Another was taken on April 26, while the patient was convalescing, and a control record was made two months later (on June 6).

Case 2.—S. D., a boy, aged 10 months, was admitted to the hospital on April 8, 1932, and discharged on April 27. He was brought because of fever for two days, with a convulsion and rigid neck preceding admission. The patient was moderately pale and appeared acutely ill. The lungs were resonant throughout; the breath sounds were vesicular, and no râles were heard on admission. The heart borders were within normal limits, and there was no displacement. The cardiac rate was fast but regular; the tones were clear, and there were no murmurs. The chief abnormal physical findings were moderate rigidity of the neck and a positive Brudzinski sign. The temperature was 104 F. Respirations were rapid. Gradually impairment of resonance was noted in the upper lobe of the right lung, which was followed finally by bronchial breathing. Signs of consolidation in the upper lobe of the right lung were confirmed by a roentgenogram. A lumbar puncture showed normal spinal fluid.

On the fourth day the temperature dropped by crisis. Following this the signs of consolidation gradually cleared up.

An electrocardiogram was taken on April 12, and a control record was made two and a half months later (June 24).

Case 3.—R. L., a white boy, aged 18 months, was admitted to the hospital on May 4, 1932, and discharged on May 17. There was a history of a "cold," with discharging ears for three weeks before admission; difficulty in breathing for one week, and vomiting, stupor and intermittent cyanosis for two days. On admission the patient was acutely ill. The temperature was 105 F.; there were rapid labored respirations with a respiratory grunt and slight cyanosis of the lips and fingers. There were bilateral purulent otitis media, dulness in the upper lobe of the right lung, with distant bronchial breathing, and occasional moist râles. There was no cardiac enlargement; the rhythm was regular, and the rate was rapid. No displacement was noted, and there were no murmurs.

The temperature was irregular for the first five days; it gradually dropped by lysis to normal on the seventh day, after which it remained normal.

Electrocardiograms were taken on May 6, 7, 8, 12 and 15, the last record being taken when the child was well.

Case 4.—R. R., a Mexican girl, aged 3 years, was admitted to the hospital on March 24, 1932, and was discharged on May 4. There was a history of fever and anorexia for one week and cough for two days. On admission the temperature was 104 F. The patient was not acutely ill. She had impairment of resonance over the lower lobe of the left lung, with some diminution of breath sounds over this area. No râles were heard. The heart borders were within normal limits, and there was no displacement. The sounds were of good quality; no murmurs were audible.

On the day following admission the temperature rose to 106 F. and was irregular for the following eight days. Dulness became marked at the base of the left

lung, and bronchial breathing and crepitant râles also became marked in this area. The pulmonary condition gradually cleared up.

A roentgenogram taken on March 25 showed consolidation of the lower lobe of the left lung. A repeat roentgenogram taken on March 31 showed consolidation still present in this area. Eventration of the right leaf of the diaphragm took place, with most of the stomach herniating into the right pleural cavity.

Electrocardiograms were taken on March 29, when the patient was acutely ill, and again on April 5.

CASE 5.—B. V., a white boy, 4 years of age, was admitted to the hospital on May 15, 1932, and was discharged on May 25. There was a history of cough for five days and fever, with difficulty in breathing for three days. Examination showed a moderately ill child with a temperature of 104 F. There was dyspnea but no cyanosis. Percussion showed dulness at the lower lobe of the left lung posteriorly, with tubular breathing and crepitant râles in that area. The heart was not enlarged. There was no displacement; the sounds were of good quality, and there were no murmurs.

The temperature dropped by lysis to normal on the fifth day. The child was never extremely ill.

Electrocardiograms were made on May 17, 20 and 27. The first two tracings were made during the acute stage; the last was the control record.

CASE 6.—J. S., a boy, aged 5 months, was admitted to the hospital on May 5, 1932, and was discharged on May 26. The patient became listless three days before admission, refused to nurse and looked quite ill. In addition, the parents noted that his breathing was noisy and rapid and that he coughed frequently. One day before admission the child's lips were noted to be blue. Examination revealed an acutely ill child, prostrated and breathing rapidly. The lips were cyanotic. The heart was within normal limits, and there was no displacement. The heart tones were of good quality, and the rhythm was regular. There was a long, loud blowing systolic murmur over the entire precordia. The right lung showed impairment of resonance over the upper lobe posteriorly, with bronchial breathing and fine crepitant râles over this area. In addition, there were medium moist crepitant râles at the base of the left lung posteriorly.

For four days the temperature was irregular; it dropped by lysis on the fifth day. The diagnosis of bronchopneumonia was confirmed by roentgenograms.

Electrocardiographic tracings were made on May 7, 9, 12, 15 and 18, and a final record was made on May 21, after recovery.

CASE 7.—J. C., an 8 month old boy, who was admitted to the hospital on May 6, 1932, and was discharged on May 27, had been well until four days before admission, at which time the mother first noticed fever, irritability and a nasal discharge. The following day a cough developed. Two days before admission the patient's respirations had become rapid and were accompanied by dilatation of the alae nasi. On the day of admission cyanosis was noticed, and the patient became stuporous and difficult to arouse. The temperature was 106 F., and respirations were 64. The patient was acutely ill, with rapid, labored respirations and marked apathy. The skin had a grayish pallor, and the lips were cyanotic. The alae nasi were dilating with each respiration. There was some impairment of resonance over the upper lobe of the left lung posteriorly, with many moist, crepitant râles over both lungs, both anteriorly and posteriorly. The heart borders were within normal limits. The tones were of good quality; the rhythm was regular, and no murmurs were heard. The abdomen was distended and tympanitic. The impression was that of severe bronchopneumonia. Immediately after admission the

patient was placed in an oxygen tent. He had a high temperature for five days and then had low grade irregular fever for nine more days. A complication arose in the form of otitis media on the left side, which subsided without paracentesis.

Electrocardiograms were made on May 10, 12, 16, 18, 20 and 22, and the control tracing was made on May 27.

CASE 8.—L. S., a white girl, aged 7 years, was admitted to the hospital on Nov. 7, 1931, and was discharged on November 24. The patient entered because of fever for one week, cough for two days, and pain in the chest for one day before admission. Two weeks before admission she had had a slight cough, which had improved after three days. She then did well until eight days before admission, when she had a chill, followed by a high temperature. Six days later a cough developed, and the day before entry there was pain throughout the chest on coughing. Examination revealed an acutely ill white girl, aged about 7 years. Her condition was markedly toxic, and there was some cyanosis. The throat was injected. There were dulness at the base of the left lung posteriorly, with bronchial breathing and bronchophony, and medium moist, crepitant râles throughout both lungs. She was placed in an oxygen tent immediately after admission.

On November 9 her condition became much worse. She was delirious, restless and quite cyanotic. There were still dulness, bronchial breathing and râles at the base of the left lung. The temperature was 105.4 F.; the pulse rate, 120, and the respiratory rate, 60.

On November 10 the patient was still cyanotic. Respirations were relatively slow and shallow. The temperature dropped to 97.2 F.; the pulse rate was 120, and the respiration rate was 30; the condition was critical.

On November 11 the condition was somewhat improved. The temperature rose to 104 F. at midnight and fell to 99 F. by rectum at noon. There were now crepitant râles present at the bases of both lungs. On November 12 the patient's condition was better but was still toxic. The face was flushed; the temperature was 101.6. F. by rectum; the pulse rate was 102, and respirations numbered 42. On November 13 there was considerable improvement in the patient's condition; there was no cyanosis and no dulness. There were still many medium, moist crepitant râles over the bases of both lungs. The patient was taken out of the oxygen tent for a short time. On November 14 a few patches of bronchial breathing and bronchophony were audible at the base of the left lung posteriorly. Râles were still present at the bases of both lungs. The oxygen tent was to be removed.

On November 16 the patient was better; there was no cyanosis, and the condition of the chest was clearing up. On November 17 considerable improvement was noted; there were a few scattered râles at the bases of both lungs. On November 18 the patient was afebrile, and the condition was good. On November 20 the chest was clear, and the patient was convalescing.

In all, ten electrocardiograms were made, on November 11, 12, 13, 14, 15, 16, 17, 18 and 19, and a final control record was made on April 25, 1932.

ANALYSIS OF ELECTROCARDIOGRAMS

The data are summarized in the table, and segments of typical curves are shown in figures 1, 2 and 3.

Rate and Rhythm.—Increases were noted in the cardiac rate during the febrile periods of the disease, and transient bradycardia occurred

Changes in Electrocardiograms During Acute Pneumonia as Compared with the Control Tracing *

Case	Rate†	P R Interval	P Wave	Q R S Complex	S T Interval	Shift of Axis	T Wave
1	A, 188 B, 167	No change	Smaller in lead I	Amplitude smaller in all leads; no change in duration	No change	No change	Smaller and shorter in lead I; smaller, tends to be shorter, in lead II; slightly positive, whereas in control tends to be slightly negative in lead III
2	A, 125 B, 112	0.02 second shorter	No change	No change	No change	No change	Smaller in lead I; smaller in lead II; slightly less negative during acute illness and in control, in lead III
3	A, 167 B, 125	0.02 second longer	Larger in leads I and III	Q wave in leads II and III; same slurring in lead III; amplitude increased	Leads I and II, no change; lead III, slightly positive; same in control	No change	Smaller and shorter, with rounded summit, in lead I; smaller, shorter and rounded in lead II; fluctuates around normal in lead III
4	A, 143 B, 125	No change	Smaller in lead I, larger in lead III	Amplitude less	Slightly positive; in control lead I; no change in leads II and III	No change	Smaller in lead I; smaller and rounded in lead II; slightly taller in lead III
5	A, 100 B, 78	0.02 second shorter	No change	No decided change	No change	Tendency toward shift to right	Slightly taller and shorter in lead I; smaller in lead II; slightly smaller in lead III
6	A, 167 B, 150	No change	No change	Smaller	S T looks slightly negative—may be due to P wave climbing on T	Tendency toward shift to right on occasion	Smaller and less peaked in lead I; smaller, except in one stage, where it is larger than normal, in lead II; smaller in lead III
7	A, 167 B, 136	0.04 second shorter	Smaller in all leads	Q R S_1, smaller; Q R S_2, smaller; Q R S_3, no change; occasional slurring in leads I and III	Iso-electric in all leads; control positive in leads I and II	No change	Smaller in lead I; smaller and shorter in record of 5/10/32, and almost nondiscernible in lead II; smaller and on two occasions slightly negative in lead III
8	A, 100 B, 75	0.04-0.08 second longer	No consistent change	Occasional slurring	Occasionally positive in lead III	No change	Negative to varying extents, whereas small and positive in control, in lead I; smaller and shorter (diphasic in two records) in lead II; varies—in some records larger than control, in others, smaller (negative once) in lead III

* Smaller and taller refer to the height of the various waves, and longer and shorter refer to the duration of the waves.
† A denotes the rate during the acute illness; B, the rate in the control record.

several times during convalescence. In case 8 of our series, oxygen therapy at one time seemed to slow the rate, but similar temporary slowing occurred later when the patient was out of the oxygen tent, which might indicate a varied vagus balance during pneumonia. Sinus arrhythmia was more pronounced in the afebrile convalescent stage than during the acute disease (fig. 1).

P R Interval and P Wave.—A slight shortening of the P R interval was noted several times during the acute pneumonia, and was probably

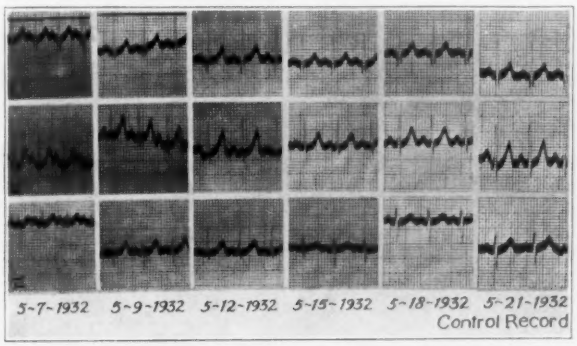

Fig. 1.—Segments of serial electrocardiograms in case 6.

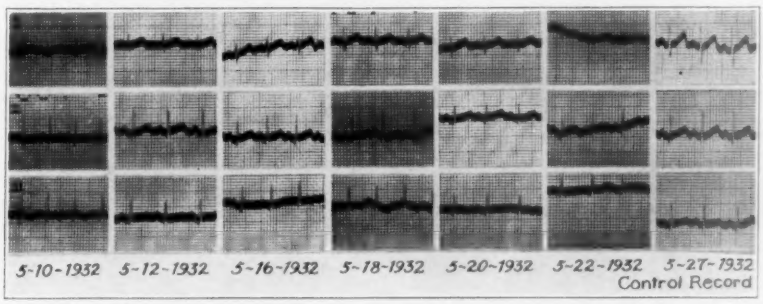

Fig. 2.—Segments of serial electrocardiograms in case 7.

associated with the accelerated rate accompanying pyrexia. However, in two instances a prolongation of the P R interval was noted during the acute illness; in one the increase was to 0.24 second, indicating a definite auriculoventricular block, which disappeared after convalescence, as was demonstrated by the control records.

The changes in the P wave were, on the whole, insignificant, with slight variations in size and no invasions.

Q R S Complex.—There was slight slurring in a number of the Q R S components (figs. 1 and 3). No increase in duration was noted,

with the exception of a slight increase in one record of case 8, and this was within normal limits.

S T Interval and T Wave.—There were only minor changes in the S T interval, which could in no way be interpreted as deviations from normal limits. However, in every case there were some changes in the T wave. In leads I and II the T waves became smaller and less peaked during the acute illness. In case 8 the T_1 and T_2 waves were inverted, and in one record they showed a suggestive cove shape (fig. 3, lead I, Nov. 16, 1931).

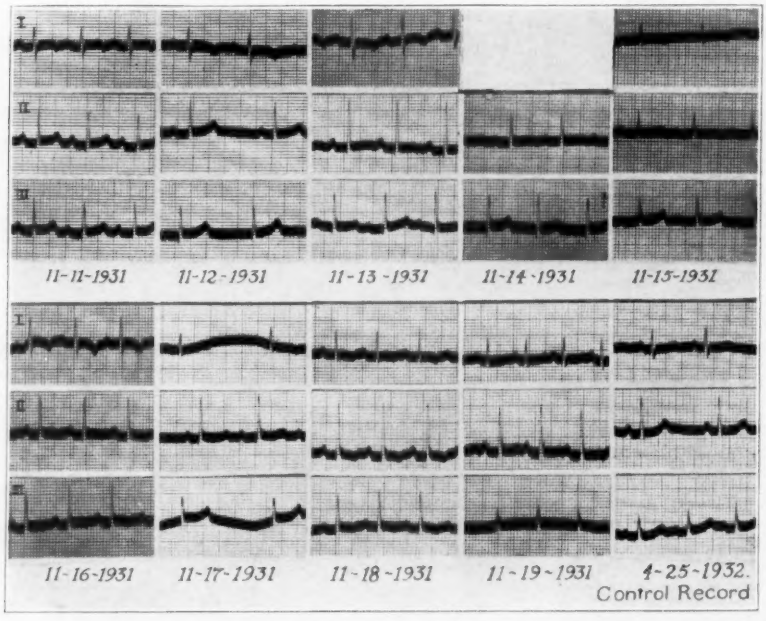

Fig. 3.—Segments of serial electrocardiograms in case 8.

The T waves of lead III showed changes less constant than those noted for T_1 and T_2. It should be remembered that the contour of T_3 is variable in healthy infants and children.[1]

In general, the changes in the T wave were most marked in those records in which abnormalities were noted in the other components of the electrocardiogram.

Electrical Axis Shift.—A shift in the axis to the right was noted in the records of two patients (fig. 1 and cases 5 and 6 in the table).

SUMMARY OF POSITIVE FINDINGS

The most pronounced changes in the electrocardiographic records during the acute pneumonia in the infants and children here studied

occurred in the P R interval and in T_1 and T_2. In two instances there was a definite prolongation during the acute stage to as much as 0.24 second, or a definite auriculoventricular block. Every case showed some changes in the T wave, particularly in leads I and II: this wave became smaller and less peaked during the acute illness, and was inverted and cove-shaped in one case. The changes in T_3 were less constant and are of less significance in children (table). A shift of the electrical axis to the right occurred twice.

COMPARISON WITH ELECTROCARDIOGRAPHIC CHANGES IN PNEUMONIA IN ADULTS

The prolongation in the auriculoventricular conduction in this series occurred during the acute stage of the disease, while the changes reported by Master[6] in the adult series occurred after the patient had become afebrile and was beginning to convalesce. Changes in T_1 and T_2 occurred more frequently in the infants and children than in the adult patients. The changes in the S T interval were notable in the adult series; they were not marked in our group. Neither premature beats nor fibrillation occurred in this series, while these irregularities were noted several times in the adults. It is noteworthy that the electrocardiographic abnormalities which we have pointed out in the tracings of the infants and children studied occurred only during the acute pneumonic process and disappeared during convalescence, which is in contrast to some of the findings for adults. Further, the changes noted were actual abnormalities for those persons, as they were not present in the control records after recovery from the illness.

COMPARISON WITH ELECTROCARDIOGRAPHIC CHANGES IN OTHER DISEASES

The changes in the electrocardiogram reported in rheumatic fever and rheumatic carditis may become persistent and constant. They include increased auriculoventricular conduction time, changes in the P waves, slurring and prolongation of the Q R S complex, absence of an iso-electric S T interval in lead II and minor changes in T_2 and T_3. In diphtheria, electrocardiographic changes indicative of myocardial involvement have been noted in mild cases during the early part of the disease. Many children have shown normal tracings after recovery. Frequently these changes in the electrocardiogram have been noted when no physical signs of cardiac involvement were present. In more severe cases, abnormalities in conduction have been noted, varying from a slight increase in the P R interval to a complete block with an independent ventricular rhythm, which have remained permanent in many instances. The changes in the electrocardiogram thus far reported

in scarlet fever showed no prolongations of the P R interval and only minor changes in the T wave in 10 per cent of the children. These slight changes returned to normal during convalescence. It is evident that the electrocardiographic changes in acute stages of scarlet fever, mild diphtheria and pneumonia are transient. Permanent changes occur following rheumatic infection and severe cases of diphtheria. The electrocardiographic changes observed during pneumonia are less marked than those noted in severe cases of diphtheria and rheumatic disease, but are more marked than those reported for scarlet fever. Hamburger and Priest [7] found prolonged conduction time and bundle branch block at the height of acute respiratory infections. Von Kiss [8] recently reported bundle branch block and flattening of T waves in infants with grip.

COMMENT

The changes in the auriculoventricular time and in the T waves noted in the serial electrocardiograms taken during the acute pneumonia here described might be explained by a nervous or a chemical change, by changes in the position of the heart or diaphragm, by the influence of electric conduction by a consolidated lung, or anoxemia, or by toxic or actual myocardial involvement during the acute disease.

Few facts are known as to the chemical changes occurring in pneumonia in infants and children. Abt [9] pointed out that creatine and uric acid are found to be increased in the urine in acute pneumonia and that the nonprotein nitrogen of the blood serum is also increased.

Gerstenberger [10] and others found hypocalcemia and decreased values for inorganic phosphorus in children with pneumonia. Kramer and Tisdall [11] reported that potassium may be decreased at times, though it may be normal. Retention of sodium chloride has been noted, with an increased excretion of acids in the urine, and it has even been suggested that a certain degree of acidosis may exist in pneumonia. It is doubtful whether these chemical changes affect the electrocardiogram.

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7. Hamburger, W. W., and Priest, W. S., Jr.: Structural and Functional Involvement of the Heart Following Acute Respiratory and Other Acute Infections, Tr. A. Am. Physicians **38**:97, 1923.

8. von Kiss, Paul: Ueber die Herzstörungen im Verlaufe der Säuglingsgrippe, Monatschr. f. Kinderh. **56**:83, 1933.

9. Abt, I. A.: Round Table Conference on Pneumonia, J. Pediat. **2**:104 (Jan.) 1933.

10. Gerstenberger, H. J.; Burhans, C. W.; Smith, D. N., and Wetzel, N. C.: Blood Serum Content of Inorganic Phosphorus and Calcium in Pneumonia, Am. J. Dis. Child. **26**:329 (Oct.) 1923.

11. Kramer, B., and Tisdall, F. F.: Clinical Method for Quantitative Determinations of Potassium in Small Amounts of Serum, J. Biol. Chem. **46**:339 (April) 1921.

Wallgren [12] and Griffith [13] noted a temporary displacement of the heart toward the affected side and a high position of the diaphragm on that side. At the time of resolution the normal positions are resumed. No cardiac or diaphragmatic displacements were noted by physical signs in our patients or in those patients of whom roentgenograms were made.

The exchange of gases in the lungs is considerably affected in pneumonia, and during the febrile period there is an increased consumption of oxygen. The consolidation of a portion of the lung, coupled with interference with arterial circulation, tends to produce anoxemia. Katz and Wallace [14] showed that anoxemia produces marked changes in the electrocardiogram. Anoxemia may be the cause of the electrocardiographic changes here described.

The electrocardiographic changes are more probably due to toxic myocardial changes, and therefore we should consider a temporary toxic myocardial involvement during acute pneumonia as the most plausible explanation of our results. The patient in case 8 was the most toxic of our patients and was thought to have shown clinically some cardiac involvement. The changes in this series of tracings were likewise the most pronounced of those in the cases studied. The electrocardiographic changes noted in the other patients are probably a more delicate index of cardiac involvement than could be determined by clinical facts or physical signs.

CONCLUSIONS

1. Serial electrocardiograms were taken on infants and children with acute bronchopneumonia on successive days of the illness, and the tracings taken during the acute illness were compared with a control record taken after complete recovery. The changes noted in the tracings during the acute illness were actual abnormalities for the individual infants and children studied.

2. The electrocardiograms here reported were made on infants and children from 4 months to 7 years of age, all ill with acute bronchopneumonia. There were no fatalities in the group studied, and no patient received any drug capable of altering cardiac conduction or affecting the heart muscle.

3. The electrocardiographic records showed most pronounced changes in the P R interval and the T waves in leads I and II. The

12. Wallgren, Arvid: Displacement of Heart in Pneumonia, Acta pædiat. **3**:81, 1923.

13. Griffith, J. P. C.: Displacement of Heart in Pneumonia in Children, Am. J. M. Sc. **174**:448 (Oct.) 1927.

14. Katz, L. N., and Wallace, A. W.: The Rôle of Cardiac Ischemia in Producing R-T Deviations in the Electrocardiograms, Am. J. M. Sc. **181**:836 (June) 1931.

P R interval was definitely prolonged in two instances during the acute disease. In one instance an auriculoventricular block of 0.24 second was established. Every case showed some changes in the T wave in leads I and II; in one case the T waves were inverted, and in one record they were cove-shaped. A shift of the axis to the right occurred twice.

4. The changes established in the electrocardiogram in acute bronchopneumonia in infants and children were compared with electrocardiographic changes found in pneumonia in adults and also with those found in rheumatic disease, diphtheria, scarlet fever and acute respiratory diseases.

5. The possible causes of the electrocardiographic changes are enumerated. The evidence suggests an actual toxic myocardial involvement in acute bronchopneumonia in infants and children.

6. The electrocardiographic changes noted are probably a more delicate index of cardiac involvement than could be determined by clinical facts or physical signs in the majority of the cases here reported.

104 South Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. LOUIS N. KATZ, Chicago: It is not generally realized that during acute infections changes in the spread of the impulse throughout the heart and in the irritability of various parts of the myocardium may give suitable evidence that the heart is involved. In such cases an idea of the presence of damage to the heart may be obtained by following, as Dr. Abt and Dr. Vinnecour did, the daily changes in the electrocardiogram. Extrasystoles will indicate irritable foci. Changes in the P R interval will indicate alterations of the conduction time from auricles to ventricles, and changes in the T wave, the S T interval and the Q R S complex will give evidence of disturbances of intraventricular conduction. This sort of study is valuable not only in pneumonia but in other infectious diseases, such as scarlet fever, diphtheria and acute rheumatic fever. When properly evaluated, it may give more valuable information about the condition of the heart than physical examination.

It must be borne in mind, of course, that the electrocardiogram does not show how well the heart is contracting, except inferentially by showing evidence of damage to the heart.

Damage of the heart in these infections may not be due to the inflammatory process alone. It may be caused by an insufficient supply of oxygen to the heart, by "toxins" or by the pyrexia. It may be permanent or transient.

Studies such as that of Dr. Abt and Dr. Vinnecour suggest that the electrocardiogram offers a profitable means of approach in studying the heart in acute infections.

DR. M. H. NATHANSON, Minneapolis: Electrocardiography was first utilized almost entirely in cases of irregular hearts. Later it was applied to the study of chronic myocardial conditions, particularly to give an idea of myocardial changes in vascular diseases of the heart, such as coronary disease. Only recently has it been applied to the study of acute infections.

Four years ago I studied a group of patients with diphtheria and found extreme changes in the electrocardiograms during the acute stage, such as deep inversions of the T wave, which persisted during convalescence and for from six to eight weeks after the patient was clinically well, and which returned to normal only gradually.

We make it a rule at the Minneapolis General Hospital in severe cases of diphtheria to take routine electrocardiograms, and patients who show inversions of the T wave are kept flat on their backs until the electrocardiogram shows a normal reading. In the only two cases in which death apparently occurred from heart failure the patients showed these electrocardiographic changes and left the hospital against advice.

Studies such as this have an important bearing on the question of the pathologic physiology of the circulation in infections. For more than thirty years there have been two theories as to the mechanism of circulatory collapse in an infection. One school thought that the heart was primarily involved; the other school thought that the changes were in the blood vessels.

These electrocardiographic studies indicate that a change in the myocardium is produced by bacterial toxins. However, I think that there must be some care in interpreting this. There is very little doubt that a bacterial toxin affects both the heart and the blood vessels. In certain diseases, such as diphtheria, which show high grade electrocardiographic changes, the pathologic changes are most intense in the myocardium. However, when one sees a patient with pneumonia in collapse, with a blood pressure of almost zero or of only 30 or 40 mm., with a rapid pulse, and when there are only minor changes in the electrocardiogram, one is fairly certain that the change is not primarily cardiac but is in the blood vessels.

Dr. Arthur F. Abt, Chicago: I wish to thank Dr. Katz and Dr. Nathanson for their discussion. We are indebted to both for their work in cardiovascular disease.

The changes which I found are not pathognomonic of pneumonia. They occur also in other infectious diseases. They are, in some instances, more delicate than the physical signs and symptoms would indicate. The results of this study, so far as I can see, suggest nothing new in the way of therapy.

CLINICAL RADIOSCOPIC STUDIES OF THE HEART IN CHILDREN

ROENTGENOLOGIC CRITERIA OF CARDIAC ENLARGEMENT; SIZE OF ANGLE OF CLEARANCE OF LEFT VENTRICLE AS CRITERION OF VENTRICULAR ENLARGEMENT

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The markedly enlarged heart is easily recognized by physical and roentgenographic examination. The differentiation between the normal and the moderately enlarged heart in a child presents a diagnostic problem of clinical importance. The usual roentgenologic criteria offer little assistance in determining the most important single criterion of early organic heart disease, namely, enlargement of the heart.

This investigation was undertaken to evaluate certain roentgenologic criteria of cardiac size in children. In addition, an effort was made to define, if possible, criteria to detect slight or early cardiac abnormality by a roentgenologic method which would be simple, rapid, reasonably accurate and available for clinical use.

METHOD

Of the roentgenologic methods in general use the first is estimation of the size of the heart by mensuration of the frontal plane as projected by teleoroentgenography,[1] teleoradioscopy [2] and orthodiagraphy.[3] The measurements of these cardiograms are related to certain bodily measurements; and enlargement of the heart is determined by comparison with normal standards or a range of normal values established by various observers.[4] The second method is fluoroscopic examination of the

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From the Department of Pediatrics, Cornell University Medical College, and the New York Hospital.

1. Roentgenograms are taken with the tube at a distance of two meters (frequently from 6 to 7 feet). The errors of projection are not considered significant.

2. Cardiac outlines are traced directly on a fluorescent screen or on tracing paper. The tube is at a distance of 2 meters.

3. The cardiac outline is followed by the central ray of the x-ray cone giving the accurate size of the heart.

4. (*a*) Bardeen, C. R.: Tables for Aid in the Determination of the Relative Size of the Heart by Means of Roentgen Ray, Am. J. Roentgenol. **4**:604, 1917. (*b*) Danzer, C. A.: The Cardio-Thoracic Ratio. An Index of Cardiac Enlargement, Am. J. M. Sc. **157**:513, 1919. (*c*) Kissane, R. W.: Area of the Body Surface and Measurements of the Normal Heart in Children: II. Roentgen Study, Arch. Int. Med. **45**:241 (Feb.) 1930. (*d*) Vaques, H., and Bordet, E.: The Heart and the Aorta, Studies in Clinical Radiology, New Haven, Conn., Yale University Press, 1920.

heart, the subject being placed in various positions. Abnormality is judged by a change in the configuration, size and position of the cardiac chambers from the normal.[5]

The roentgenologic method finally selected was radioscopy, which included teleoradioscopy and fluoroscopy. Comparative examinations were made by teleoroentgenography in a small series.

Cardiograms for mensuration of the cardiac silhouette secured in the frontal plane were obtained in the following manner. A special stand with a fluorescent screen was placed at a distance of 2 meters.[6] All the examinations were made with the child facing the screen directly in front of the fluoroscope; the cardiac silhouette was rapidly drawn (during normal respiration) on transparent paper. The points necessary for mensuration were identified and marked, and the cardiograms were measured in the usual manner.[7] These cardiograms represent less accurately the size of the frontal plane of the heart than do orthodiagrams. Teleoradioscopy was selected as a more practical method for the examination of children. It is rapid and permits simultaneous visualization of the entire cardiac silhouette. This is a great advantage, as the slightest movement of the child can be detected. With both radioscopic methods the cardiac borders may be more easily and accurately followed on the fluorescent screen than is possible on roentgenograms.

The two criteria of size of the heart selected for study were the cardiothoracic index,[4b] which is the one most frequently used, and the cardiac surface area.[8] The latter was related to the body surface area,

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5. Nemet, G.: Guide to Radiologic Diagnosis in Heart Disease, The Heart Committee, New York Tuberculosis and Health Association, 1930.

6. The stand permitted the screen to slide vertically and to be fixed at various heights. The tube and screen were accurately adjusted at various heights by means of fixed rulers on both the stand and the fluoroscope. A Coolidge fine focus tube was used. Short exposures of less than thirty seconds were given. An amperage of 5 milliamperes gave sufficient penetration. This stand is also suitable for orthodiascopic examination.

7. The transverse diameter of the chest was measured at the inner sides of the ribs at the level of its greatest diameter above the diaphragm. The right auricle and left ventricle were identified and the upper border freely drawn; the lower border was usually visualized and traced directly. The greatest right and left diameters of the heart were measured. The surface area of the heart was obtained by the use of a Dietzgen planimeter. The area of the body surface was calculated from the Du Bois chart, Proc. Soc. Exper. Biol. & Med. **13**:77, 1916.

8. The teleoroentgenograms studied were taken by Mr. T. Brott and Miss R. Pidgeon, through the courtesy of Dr. J. R. Carty, Director of the Department of Radiology, the New York Hospital.

and a quotient was derived from that relationship.[9] These two measurements represent the size of the frontal plane of the heart as projected by roentgen rays.

Fluoroscopic examination was made with the subject in the following three standard positions, namely, posterior anterior (the subject facing the screen), left anterior oblique (left shoulder to the screen) and right anterior oblique (right shoulder to the screen), in the order named.

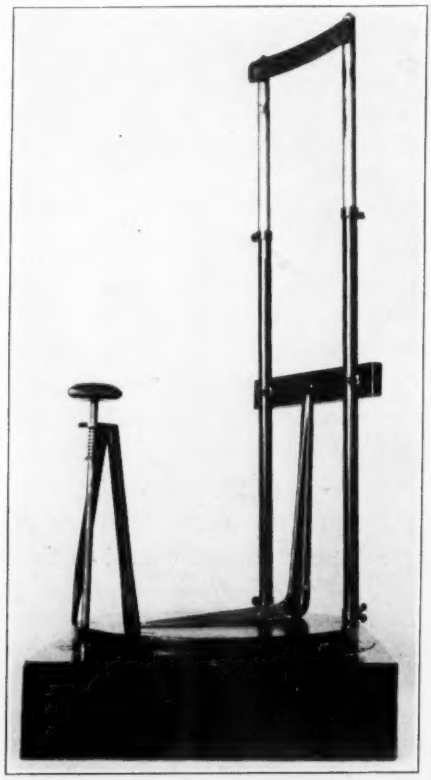

Fig. 1.—Turntable. Left anterior oblique position at 50 degrees of rotation.

The contour of the heart and the extent of the retrocardiac space vary with the obliquity of the body. It was therefore desirable to know the degree of rotation in the oblique positions. A turntable [10] was used.

9. The surface area was selected rather than height or weight as it has been observed that the surface area of the body gives the highest coefficient of correlation when compared with other bodily measurements (Josephi, M. J.: Measurements of the Size of the Heart in Normal Children: A Statistical Study, to be published).

10. The revolving platform was calibrated from 0 to 90 degrees at its circumference on each side of the median line. In the anterior position zero was centered (fig. 1).

The child was instructed to stand erect on the revolving platform facing the screen and cautioned not to move. In the latter part of the study the degree of obliquity of the body was simultaneously measured at the level of the biscapular axis with a goniometer [11] in order to check the accuracy of the degree of rotation. Certain children tend to resist rotation and move about; therefore it is frequently advisable to observe a child during rotation. The majority of the children cooperated, and repeated examinations gave consistent results. Three or more examinations were made of each subject.

Familiarity with the normal cardiac silhouette in these positions is essential. Detailed descriptions and illustrations of the normal configuration of the heart may be found in numerous publications [12] and

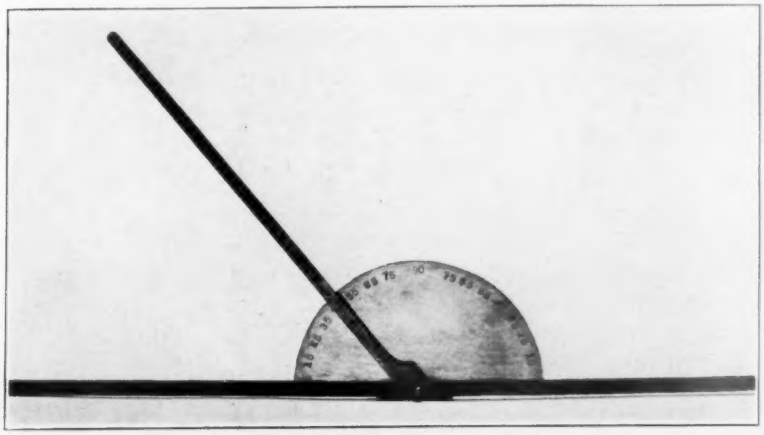

Fig. 2.—Goniometer at 50 degrees.

will not be considered here. In this study the following observations were made: In the posterior-anterior view the cardiac silhouette was inspected from above downward; on the right lateral border above for abnormal pulsation in the region of the superior vena cava and aorta, and below for the increased saliency of the right auricle; on the left lateral border from above downward for the contour of the aortic arc, pulmonic arc, pulmonary conus and left ventricle.

In the left anterior oblique position, the subject was rotated until the dorsal border of the heart below (which is the left ventricle) was clearly separated from the vertebral column (about from 0.2 to 0.5 cm.) in

11. The goniometer consisted of a rule pivoted on a divided dial and a second fixed rule fastened to either the screen or the stand of the fluoroscope. In the oblique positions, the movable rule was placed against the chest at about the level of the second intercostal space, and the degree of obliquity was ascertained (fig. 2).

12. Vaques and Bordet.[4d] Nemet.[5]

normal respiration. The degree of rotation at which this was observed was arbitrarily designated as the angle of clearance of the left ventricle.[13] In addition, the left auricle above was inspected for enlargement by identification of the angle of bifurcation of the trachea. The ventral border of the heart in this position, outlining from above downward the right auricle and the right ventricle, was also observed for change in contour.

In the right anterior oblique position sufficient rotation (at least to 55 degrees) permitted visualization of the dorsal border of the heart, which is mainly the left auricle separated from the vertebral column. To differentiate the left auricle from the hilar shadows it was found necessary to give a teaspoonful of a mixture of chocolate and barium sulphate of thick consistency to outline the esophagus. Slight enlargement of the left auricle (causing retrodisplacement of the esophagus) was recognized by this procedure. The ventral border of the heart in this position, particularly the pulmonary conus, was inspected.

Tracings of the cardiac silhouette in these positions were drawn on transparent paper for permanent records. These cardiograms do not represent the actual size of the heart. In order to evaluate the significance of the enlargement of the cardiac silhouette due to the marked divergence of the rays during fluoroscopy (a distance of about 2 feet), comparative teleoradioscopic examinations at a distance of 2 meters and teleoroentgenographic examinations at a distance of 7 feet (where the rays are more parallel) were made of 60 of these subjects at standard degrees of rotation.[8]

SUBJECTS

Five hundred and four children from 5 to 15 years of age were included in this study. Of these, 119 were average normal children selected from a private school and from a clinic;[14] 61, children in whom there was possible cardiac disease (without evidence of enlargement or characteristic murmur, the majority having systolic murmurs in the second left intercostal space or at the apex); 64, subjects with potential heart disease (all of these had a past history of rheumatic fever, and many

13. Determination of the size of the angle of clearance of the left ventricle in children exhibiting postural derformities (scoliosis, kyphosis and lordosis) is difficult and may be impossible. It is obvious that these postural defects influence the normal position of the vertebral column and the dorsal border of the heart in the oblique position. In this study it was found practical to interpolate an imaginary line of continuation for the normal vertebral curve. It is also evident that displacement of the heart to the left, due to effusions or adhesions, will interfere with the accuracy of this criterion.

14. These children were found to be free from evidence of heart disease on physical examination and did not have in their past histories factors predisposing to cardiac disease. Dr. L. Schoenthal and Dr. M. I. Levine selected and examined these children.

had inconstant systolic murmurs or impure first sounds at the apex); 45, children with congenital cardiac defects, and 215, children with chronic cardiovalvular disease.[15]

OBSERVATIONS

An analysis of the data secured for 119 normal subjects will be considered first.

Eighty-four per cent of the children showed a cardiothoracic index of less than 50 per cent. Ninety-eight per cent showed a body surface—cardiac surface area quotient of 14 or more.[16]

On fluoroscopic examination in the posterior anterior position the heart was in the transverse position in 44 per cent of the subjects and in the vertical in 56 per cent. About one-half showed one or more of the following abnormalities: prominent pulmonary arc, 8 per cent; increased pulsation at the base, 15 per cent; slight fulness of the pulmonary conus, 27 per cent; marked convexity of the pulmonary conus, 5 per cent; and straight left cardiac border, 19 per cent. In average normal children these observations must be considered in evaluating the findings in heart disease.

On rotation in the left anterior oblique position, it was found that in 49 per cent the angle of clearance of the left ventricle was from 40 to 45 degrees; in 48 per cent, 50 degrees, and in 3 per cent, 55 degrees or more. In 97 per cent an angle of clearance of less than 55 degrees was secured. Hearts vertically placed were more likely to clear at 40 and 45 degrees.

On rotation to 55 degrees in the right anterior oblique position displacement of the esophagus was not observed.

The consistent results secured on repeated examinations in these normal subjects permitted comparison with comparable examinations of children with possible, potential and organic heart disease. These observations are summarized in the table and in figure 3.

If it is assumed that the radioscopic studies of the 119 normal subjects are representative roentgenologic observations for the normal heart in childhood, it is possible to define the following criteria of judging cardiac abnormality (as a basis for comparison) in a series of children with heart disease:

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15. The clinical diagnosis was based on Bainton, J. H.; Levy, R. L.; Manley, W. C., and Pardee, H. E. B.: Criteria for the Classification and Diagnosis of Heart Disease, Heart Committee of the New York Tuberculosis and Health Association, Inc., New York, Paul B. Hoeber, Inc., 1928.

16. A statistical analysis of the values obtained for this quotient for the 119 normal subjects gave a mean of 17.2 and a standard deviation of 1.6. Using twice the standard deviation (3.2), the lower limit of the quotient was 14 for 98 per cent of the series. A similar analysis of the data of other observers gave quotients which varied consistently with the roentgenologic method used (the larger the cardiac silhouette, the smaller the quotient).

Roentgenologic Criteria (Measurements of Frontal Plane of Cardiograms [2 meters])	Normal Series (119)		Possible Heart Disease (61)		Potential Heart Disease (64)		Organic Heart Disease: Congenital Defects (43)		Organic Heart Disease: Mitral Insufficiency (148)		Organic Heart Disease: Mitral Stenosis, Insufficiency and Aortic Insufficiency (67)	
Total transverse diameter of heart / Diameter of chest =	−50 %	+50 %	−	+	−	+	−	+	−	+	−	+
Cardiothoracic index	84%	16%	93%	7%	77%	23%	56%	44%	72%	28%	47%	53%
Body surface area / Cardiac surface area = quotient	14+ 98%	−14 2%	+ 92%	− 8%	+ 68%	− 32%	+ 65%	− 35%	+ 67%	− 33%	+ 56%	− 44%
Fluoroscopic Examination												
Posterior Anterior position	Per Cent		Per Cent		Per Cent		Per Cent		Per Cent		Per Cent	
Position of heart:												
Vertical	56		41		50		38		44		44	
Transverse	44		59		50		62		56		50	
Normal silhouette	50		16		5		0		8		0	
Increased pulmonary arc	8		14		26		11		35		56	
Abnormal pulsation at base	15		22		9		82		21		15	
Pulmonary conus												
Slight convexity	27		29		53		17		35		21	
Marked convexity	5		14		12		11		25		63	
Straight left border	19		19		28		24		46		42	
Left anterior oblique position												
Angle of clearance of left ventricle												
From 40° to 45°	49		18		0		0		0		0	
From 45° to 50°	48		59		24		40		16		5	
From 55° to 65°+	3		23		76		60		84		95	
Right anterior oblique position												
Enlarged left auricle 55°	0		0		6		0		20		92	

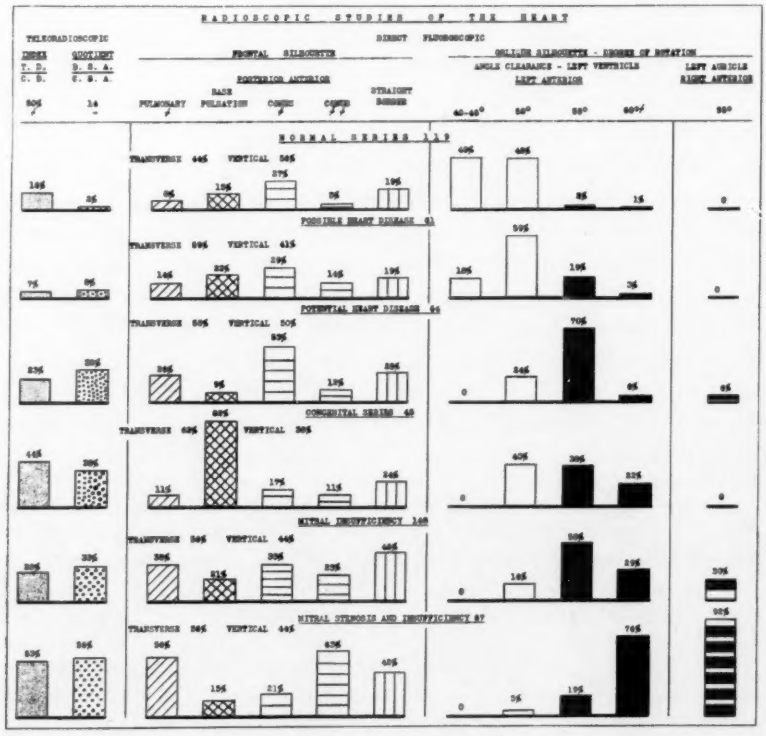

Fig. 3.—Graphic presentation of radioscopic studies of the heart.

Teleoradioscopic Examination.—1. A cardiothoracic index of more than 50 per cent and a body surface-cardiac surface area quotient of less than 14, indicating enlargement of the frontal plane of the cardiac silhouette (an enlarged right auricle, right ventricle or left ventricle, alone or combined).

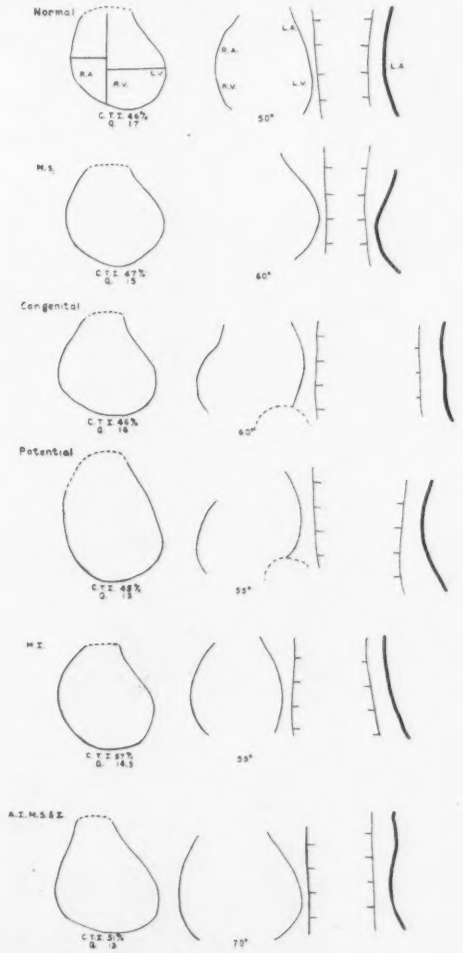

Fig. 4.—Cardiograms of the heart in the anterior and oblique positions. Column 1: cardiograms (2 meters) taken in the posterior-anterior position. *C.T.I* indicates the cardiothoracic index, $\frac{\text{transverse diameter}}{\text{diameter of chest}}$; and *Q*, the body surface area—cardiac surface area quotient. Columns 2 and 3: cardiac silhouettes traced during direct fluoroscopy. Column 2: cardiac silhouette in the left anterior oblique position at specific degrees of rotation. Column 3: cardiac silhouette in the right anterior oblique position at specific degrees of rotation.

Fluoroscopic Examination.—2. Abnormal configuration of the cardiac silhouette in the anteroposterior position: abnormal pulsation at the base, marked convexity of the pulmonary conus and a straight left border, alone or combined (indicating a congenital anomaly, right ventricular enlargement).

3. In the left anterior oblique position, an angle of clearance of the left ventricle of 55 degrees or more, indicating slight or marked left ventricular enlargement.

4. Enlargement of the left auricle: In the posterior anterior position, noted on the right lower border (marked enlargement); in the left anterior oblique position, slight enlargement at the angle of bifurca-

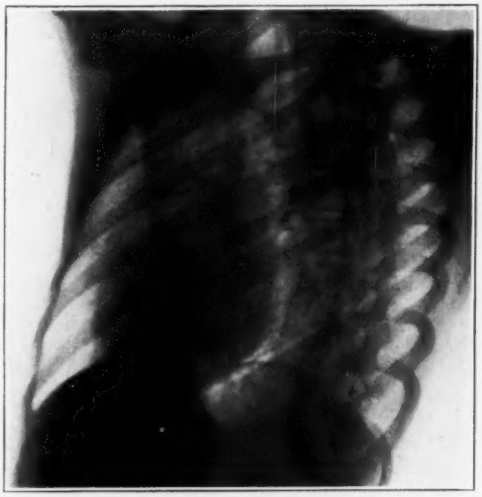

Fig. 5.—Cardiac silhouette in the left anterior oblique position in a normal child at 50 degrees of rotation.

tion of the trachea, and in the right anterior oblique position, posterior displacement of the esophagus.

A comparison of the ability of these roentgenologic criteria to differentiate cardiac abnormality in the group of children with possible, potential, and organic heart disease showed the following:

In the series of 61 subjects with possible heart disease the cardiothoracic index indicated cardiac enlargement in 7 per cent; the body surface-cardiac surface area quotient, in 8 per cent, and the size of the angle of clearance of the left ventricle, in 23 per cent.

In the group of 64 children with potential heart disease enlargement was indicated by the measurements of the frontal plane of the heart in 23 and in 32 per cent, respectively, compared with 76 per cent in whom it was indicated by the angle of clearance of the left ventricle.

Fig. 6.—Cardiac silhouette in a child (E, Dec. 6, 1932), with mitral insufficiency in left anterior oblique position at 50 degrees of rotation.

Fig. 7.—Cardiac silhouette in the same child in left anterior oblique position two months later (Jan. 28, 1933), following a recurrent carditis, at 50 degrees of rotation.

In the series of 45 subjects with congenital cardiac disease, the enlargement was indicated in 44; in 35, and in 60 per cent, respectively by these criteria.

In the group of 148 children with mitral insufficiency, enlargement of the heart was indicated in 28 and in 23 per cent, respectively, by the two frontal plane measurements compared with 84 per cent in whom it was indicated by the angle of clearance of the left ventricle.

In the series of 67 subjects with combined valvular lesions, the two frontal plane measurements, cardiothoracic index and body surface area-cardiac surface area quotient detected enlargement in 53 and in 44 per cent, respectively, compared with 95 per cent in whom the lesions were revealed by the size of the angle of clearance of the left ventricle; and, in addition, enlargement of the left auricle was noted in 92 per cent.

Analysis of the 60 teleoroentgenograms of the normal subjects as well as of the children with possible and organic heart disease confirmed the observations secured on radioscopic examination. The angle of clearance of the left ventricle was less than 55 degrees in normal children. The dorsal border of the heart, while closer to the vertebral column than in fluoroscopy (owing to the more parallel rays), was within the normal range of from 40 to 55 degrees. The size of the angle of clearance of the left ventricle does not seem to have been significantly influenced by the divergence of the rays at a distance of 2 feet.

COMMENT

The inability of the cardiothoracic index or body-cardiac surface area quotient to separate with any degree of frequency the normal from the abnormal heart in this series of observations would indicate that absolute reliance should not be placed on measurement of the frontal plane of the cardiac silhouette.[17] In addition to the many variable factors involved in such measurements is the fact that early enlargement of the right ventricle upward and to the left, the increased convexity of the pulmonary conus and the posterior enlargement of the left ventricle and auricle are not included. In marked contrast is the degree of accuracy with which it was possible to detect the abnormal heart by fluoroscopic study of the cardiac silhouette projected in several planes. Of particular interest is the large percentage of subjects with organic heart disease detected by the size of the angle of clearance of the left ventricle. The apparent ability of this roentgenologic criterion

17. The prediction tables for cardiac surface area recently published by Hodges and co-workers were found to select cardiac enlargement in about the same frequency as the body-cardiac surface area quotient (Hodges, P. C.; Adams, W., and Gordon, W.: Estimation of Cardiac Area in Children, J. A. M. A. **101**:914 [Sept. 16] 1933).

to indicate early involvement of the heart as observed in the series with possible and potential heart disease is noteworthy. It is in this type case that roentgenologic evidence of slight enlargement of the heart is most needed.

The high incidence (76 per cent) of increased size of the angle of clearance of the left ventricle in the group with potential heart disease, indicating cardiac involvement, is in accord with the belief that the heart is usually involved in rheumatic fever although the condition is not always detected on physical examination. Systolic murmurs are frequently heard in children without evidence of cardiac disease on physical examination. The low incidence (about 20 per cent) of roentgenologic evidence of cardiac abnormality observed in this group in this study is of interest.

The apparent accuracy of this criterion to detect organic heart disease in this series of observations would seem to depend essentially on its ability to indicate the presence of enlargement of the left ventricle (other factors which might influence the position of the heart being excluded). Some degree of enlargement of this chamber is usually present in organic heart disease. The early enlargement of the left ventricle is usually posterior and can therefore be seen best in the oblique position. In mitral insufficiency, left ventricular enlargement is significant; in mitral stenosis it is present, although not so prominent as right ventricular enlargement. In congenital anomalies which are not limited to the right side of the heart, particularly in those involving the ventricular septum, coincident left ventricular enlargement is present.[18]

These considerations tend to support the reliability of this roentgenologic criterion of ventricular enlargement.[19] The observations described emphasize the importance of fluoroscopic study of the various chambers of the heart. The recognition in the right anterior oblique position of left auricular enlargement in 92 per cent of the subjects with combined valvular lesions is of interest. The clinical diagnosis of mitral stenosis is frequently difficult and, as was demonstrated in this series of observations, measurements of the frontal plane of the cardiac silhouette indicated cardiac abnormality in only about 50 per cent of the cases.

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18. In the few instances of isolated right ventricular enlargement, the angle of clearance of the left ventricle would not differentiate the abnormal heart. It is possible that in marked right ventricular enlargement, the coincident posterior rotation of the left ventricle would increase the size of the angle of clearance of the left ventricle.

19. A normal angle of disappearance of the apex of the heart behind the vertebral column (from 25 to 30 degrees) in the right posterior oblique position has been defined by Vaques and Bordet [4d] as an index of ventricular volume.

It would seem justifiable to conclude from the observations secured in this study that the fluoroscopic method described gives sufficiently accurate information to arrive at an opinion as to the roentgenologic evidence of cardiac abnormality. It is a rapid, simple method which is available to the clinician, who can with little experience become familiar with the normal cardiac silhouette in children and be able to separate the normal from the abnormal heart.

SUMMARY

Radioscopic observations of 504 children between the ages of 5 and 15 years are presented. This series included normal children and subjects with possible, potential and organic heart disease.

Teleoradioscopy at a distance of 2 meters was the method used for obtaining cardiograms of the frontal plane of the cardiac silhouette for mensuration.

Fluoroscopic examination in the three standard positions, namely, posterior anterior, left anterior and right anterior oblique, was made on each subject. Standard degrees of rotation were used in the oblique positions.

From observations of 119 normal subjects the following roentgenologic criteria of judging cardiac abnormality were defined:

1. On teleoradioscopic examination a cardiothoracic index of more than 50 per cent and a body surface-cardiac surface area quotient of less than 14, indicating enlargement of the frontal plane of the cardiac silhouette (an enlarged right auricle, right ventricle or left ventricle, alone or combined).

2. On fluoroscopic examination abnormal configuration of the cardiac silhouette in the anteroposterior position: abnormal pulsation at the base, marked convexity of the pulmonary conus and a straight left border, alone or combined (indicating a congenital anomaly, right ventricular enlargement).

3. In the left anterior oblique position, an angle of clearance of the left ventricle of 55 degrees or more, indicating left ventricular enlargement.

4. Enlargement of the left auricle: in the right anterior oblique position, posterior displacement of the esophagus; in the left anterior oblique position, enlargement seen at the angle of bifurcation of the trachea, and in the posterioranterior position, marked enlargement noted on the right lower border.

A comparison of the ability of these roentgenologic criteria to differentiate cardiac abnormality showed that fluoroscopic examination differentiated the normal from the abnormal heart with the greatest frequency.

CONCLUSIONS

1. Fluoroscopic examination of the heart in children in the three standard positions is a simple, reasonably accurate roentgenologic method for recognizing cardiac abnormality.

2. The angle of clearance of the left ventricle in the left anterior oblique position differentiated with the greatest degree of frequency the normal from the abnormal heart, as compared with measurements of the frontal plane of the cardiac silhouette.

3. A normal angle of clearance of the left ventricle (of less than 55 degreees) in the left anterior oblique position would seem to be a reliable roentgenologic criterion.

TUBERCULIN OINTMENT PATCH TEST

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The tuberculin test as a diagnostic procedure is of marked importance in office practice, in the hospital and in public school work.

The intracutaneous method of applying tuberculin is recognized as the most sensitive procedure available at present, but there are definite difficulties inherent in the method which interfere with its use in some cases. The tuberculin solutions are unstable; the technic is not easy; the patients complain of the pain; the parents' consent to the test is sometimes withheld, and false positive reactions may be encountered in rare cases in the first two years of life.[1] These are some of the reasons why the application of the test is not so general as is desired, especially in private practice and in the public schools.

The Pirquet or cutaneous test has an error estimated to be 15.8 per cent (Reiss[2]); 55 per cent (Smith[3]) and 58 per cent (Hille[4]) and it does not seem to be accurate enough for general use. The test likewise has the disadvantage of requiring a certain amount of scarification.

In the past ten years various European tuberculin ointments have been used without controls. They are directly applied to the skin and as compared with the intracutaneous test have been found satisfactory concerning ease of application, stability of the preparation and sensitiveness.[5]

As no American preparation was available, I devised a tuberculin ointment which a large manufacturing concern prepared for me for

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From the Pediatric Departments of the University of California Medical School and Mount Zion Hospital.

Read before the Section of Pathology and Bacteriology of the California Medical Association at the Sixty-First Annual Session at Pasadena, May 5, 1932.

1. Duken: Unstimmigkeiten in der praktischen Verwertung der Tuberculindiagnostik, Ztschr. f. Kinderh. **43**:331, 1927. Baumler: Zur Prognose der Tuberkulose der ersten beiden Lebensjahre, Arch. f. Kinderh. **84**:136, 1928.

2. Reiss, O.: The Mantoux Reaction in Children, Arch. Pediat. **35**:714, 1918.

3. Smith, L.: Tuberculin Skin Reactions, Am. J. Dis. Child. **38**:1137 (Dec.) 1929.

4. Hille, K.: Zur Technik der perkutanen Tuberculinreaktion nach Moro, Arch. f. Kinderh. **88**:14, 1929.

5. Lovett, Beatrice R.: The Percutaneous Tuberculin Reaction, Am. J. Dis. Child. **37**:918 (May) 1929. Habstin: Die Tuberkulinsalbenpflasterprobe, Wien. klin. Wchnschr. **41**:703, 1928.

experimental purposes. It contains a highly concentrated tuberculin and killed tubercle bacilli in an ointment base. Furthermore, a control ointment was made containing the ointment base only.

The problem undertaken was to find whether this tuberculin ointment patch test including an ointment control was sensitive enough to replace satisfactorily the intracutaneous method of tuberculin testing.

TECHNIC

The area of application is the paravertebral region between the eighth and eleventh thoracic vertebrae, or the medial brachial surface.

The skin is cleansed with green soap and water, dried gently, bathed with benzene and then gently dried again. The application of benzene only, as heretofore practiced, is not sufficient to remove the secretions from very oily skins. A pea-sized drop of the tuberculin ointment is applied on the right side, and a similar-sized drop of the control ointment is applied on the left side. Each of these drops is covered with a 2 inch (5 cm.) square of adhesive tape.

READING

The test is read in forty-eight hours. The adhesive tape is removed after soaking with benzene, and the area is gently cleansed with benzene. The reaction may be clearly observed ten minutes after the removal of the tape.

Positive reactions exhibit papules, erythema, induration and pigmentation. A weak positive test shows a few (not more than twenty) discrete papules of a diameter of from 1 to 3 mm. and of a pale rose color. A medium reaction shows many vividly red papules surrounded by the skin. A strong reaction shows, in addition, changes of the total test area consisting in yellow-brown pigmentation, indurative formation of plateaus and marked reddening. A few or all of the papules may even show distinct formation of vesicles.

In weak reactions it is advisable to palpate the area in order to detect the follicles and to compare it with the area of the control.

The previously mentioned yellow pigmentation of the entire area is easily brought out by stretching the skin, whereas stretching the control area only blanches it.

COURSE OF REACTION

The peak is reached after seventy-two hours, regardless of whether the test area was covered with adhesive tape for forty-eight or for seventy-two hours. This shows definitely that the reactive substances are absorbed by the skin within forty-eight hours, and that the reaction of the skin to the absorbed material continues after the removal of the tape.

The color of the reaction begins to fade within ninety-six hours and is still faintly discernible up to one week. Medium reactions show a definite scaling up to approximately ten days, and in the marked reaction, even after two weeks, there may be roughening of the skin, brownish discolorations, infiltration and scaling of the area.

In contradistinction to the intracutaneous test, there has never, thus far, been a generalized systemic reaction such as a rise in temperature, malaise or focal signs.

Subjective symptoms accompanying the local reactions are mild. In nearly every positive case there is some itching over the test area, with only slight discomfort. In rare cases of very marked sensitiveness, slight pain over the test area may occur.

EXPERIMENTAL RESULTS

Three groups of patients were tested:

1. Fifty-nine patients in the tuberculous ward for children in the San Francisco Hospital received intracutaneous injections of 0.1 cc. of old tuberculin, 1:1,000. If the Mantoux test was negative, the

Fig. 1.—Slight positive reaction: right arm, ointment patch test; left arm, Mantoux test (1:100).

patients were retested with 0.1 cc. of old tuberculin in dilutions of 1:1,000 and 1:10.

2. Forty-three children of the Yuma Indian Reservation were tested by Dr. J. Lloyd Eaton, of Oakland, Calif., simultaneously with tuberculin ointment and 0.1 cc. of old tuberculin, 1:1,000. Dr. Eaton has shown how the ointment test as a routine procedure may give valuable results in the hands of a physician who is not familiar with the technic.

3. Eighty-eight children from the clinics for thoracic conditions of the University of California and from the outpatient department of the Mount Zion Hospital were tested simultaneously with the ointment and with intracutaneous injections of tuberculin in a dilution of 1:100. This group consisted of children who were suspected of having tuber-

Fig. 2.—Medium positive reaction: right side, positive; left side (control), negative.

Fig. 3.—Marked positive reaction of a patient with negative control: intradermal tuberculin test (right arm, human 1:100; left arm, broth control 1:100). Both reactions were positive.

culosis or who had been in contact with persons who had it. In cases of disagreement, the patients were retested with 0.1 cc. of old tuberculin, 1 : 100.

Groups 1 and 2 were also tested with an intracutaneous injection of broth used as a control. The total number of children tested was 190.

TABLE 1.—*Agreement and Discrepancies Between Ointment Test and Intracutaneous Test*

Groups	Number of Cases	Cases in Agreement, Both Tests				Cases Showing Discrepancy	
		Positive	Negative	Total	Percentage	Number	Percentage
1. San Francisco Hospital...	59	55	1	56	94.9	3	5.1
2. Yuma Indians.....	43	24	17	41	95.4	2	4.6
1 and 2 combined (human tuberculin, 1:1,000).....	102	79	18	97	95.0	5	5.0
3. Clinics (human tuberculin, 1:100).....	88	41	44	85	96.0	3	4.0
All three groups combined...	190	120	62	182	95.8	8	4.2

TABLE 2.—*Analysis of Discrepancies*

	Group	Patient	Intracutaneous Injection of Tuberculin: Human, 1:10	Human, 1:100	Human, 1:1,000	Tuberculin Ointment Patch Test	Comment
When the ointment patch test was negative and the intracutaneous injection test was positive	San Francisco Hospital	1	+	—	—	—	Ointment between H* 1:100 and 1:10
		2	..	+	—	—	Ointment between H* 1:100 and 1:1,000
	Clinics	3	..	+	—	—	Ointment between H* 1:100 and 1:1,000
	Yuma Indians	4	..	..	+	—	Ointment below 1:1,000
		5	..	..	+	—	Ointment below 1:1,000
When the ointment patch test was positive and the intracutaneous injection test was negative	San Francisco Hosp. Clinics	1	—	—	—	+	Tuberculous osteomyelitis
		2	—	—	—	+	No evidence of tuberculosis
		3	—	—	—	+	No evidence of tuberculosis

* "H" indicates tuberculin dilution.

The results of the tuberculin ointment patch test and the intracutaneous injection test are analyzed from the point of view of their agreement and from that of their discrepancies in tables 1 and 2 respectively.

As shown in table 2, 5 children gave a negative reaction to the ointment patch test and a positive reaction to the intracutaneous injection test. One of these gave a positive reaction to the Mantoux test only with a dilution of human old tuberculin of 1 : 10, 2 with a dilu-

tion of 1 : 100, and the remaining two with a dilution of 1 : 1,000. (Calcification and pleural adhesions were evident in the roentgenograms.) The last mentioned children belonged to the group of Yuma Indians who were not subjected to the injection of broth used as a control. Three children who reacted positively to the ointment patch test reacted negatively to all dilutions of the old tuberculin of the intracutaneous test. In 1, a condition was present which was diagnosed clinically as tuberculosis of the bone. In the other 2, no clinical evidence of tuberculosis was found.

Sensitivity of the Ointment Patch Test.—The high percentage of agreement (95.8) shows in general the sensitiveness of the ointment patch test. In 120 cases, the reactions to this test and to the intracutaneous test with a dilution of tuberculin of 1 : 100 were equally positive, whereas the dilution 1 : 1,000 failed to produce a positive reaction. In 1 case the dilutions 1 : 1,000 and 1 : 100 gave negative results and only the dilution 1 : 10 corroborated the positive result of the ointment test. It is thus fair to assume that the degree of reaction produced by the ointment test is generally comparable with that produced by the intracutaneous test with human tuberculin, dilution 1 : 100.

Positive Reactions to the Control.—Among the patients tested with an intracutaneous injection of the broth as a control, 27 reacted positively. In most of these the reaction to the broth was less than that to the injection of tuberculin, but in 1 or 2 it equaled the reaction to tuberculin. This makes 29 per cent with positive reactions to the broth among 96 patients of this group who gave positive reactions to tuberculin.

In contrast to this, only 4 (3.3 per cent) of the 120 patients who gave a positive reaction to the ointment test showed a reaction over the area of control, and this reaction was slight. In no case was there doubt concerning the reaction of the test.

A similar type of papular reaction was never found as a result of the use of the adhesive tape alone if it was applied for forty-eight hours.

The reasonable deduction from these figures seems to be that the nonspecific substances in the tuberculin ointment produce less reaction in the skin than do the nonspecific substances of the tuberculin solution.

SUMMARY AND CONCLUSION

1. The technic of application and the reading of the tuberculin ointment patch test and the control are described.

2. The ointment is stable and easier to apply, and it causes less psychic disturbance and less untoward general and focal reactions in the patient than does the old tuberculin used in the intracutaneous test.

3. The agreement between the ointment patch test and the intracutaneous test with tuberculin in all dilutions as performed on 190 children was 95.8 per cent.

4. The ointment patch test is generally comparable in results with an intracutaneous injection of 0.1 cc. of old tuberculin, 1 : 100.

5. The ointment patch test produced markedly less nonspecific cutaneous irritation than the intracutaneous test.

NOTE.—The Los Angeles Board of Health recently tested 685 school children with the tuberculin ointment patch test in conjunction with the Mantoux test (tuberculin dilution, 1 : 1,000). The agreement between the tests was 93.5 per cent (641 cases).

INTRANUCLEAR INCLUSIONS

INCIDENCE AND POSSIBLE SIGNIFICANCE IN WHOOPING COUGH AND IN A VARIETY OF OTHER CONDITIONS

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Whooping cough, measles and epidemic influenza are frequently complicated by a characteristic type of pneumonia which MacCallum [1] called interstitial bronchopneumonia, because the essential feature distinguishing it from ordinary lobular pneumonia or bronchopneumonia is an infiltration of the bronchial and alveolar walls by mononuclear cells. In addition to the interstitial cellular infiltration a polynuclear exudate is usually found in the central bronchiole and some of the surrounding alveoli (fig. 1). Various types of bacteria have been regarded as the cause of interstitial bronchopneumonia by different authors. In a study of pneumonia in rabbits caused by vaccine virus, Muckenfuss and McCordock [2] described infiltration of the interstitial pulmonary tissue by mononuclear cells. There has also been reproduced in animals the complete picture of interstitial bronchopneumonia as seen in man, by injecting vaccine virus with a suspension of various types of bacteria.[3] This work suggests that interstitial bronchopneumonia results from the combined action of a virus and bacteria.

Of the three human diseases complicated by interstitial bronchopneumonia, measles alone is at present generally regarded as being caused by a virus. Although the etiology of epidemic influenza is unknown, many investigators have suggested that it is primarily caused by a virus, and we regard the similarity of the pulmonary lesions to those of measles, a known virus disease, and to experimental virus pneumonia in animals as indirect evidence in support of such a view.[3] On the other hand, whooping cough is almost universally regarded as a purely bacterial disease caused by the Bordet-Gengou bacillus. Since our experi-

From the Department of Pathology, Washington University School of Medicine.

1. Cole, R., and MacCallum, W. G.: Pneumonia at a Base Hospital: II. Pathology, J. A M. A. **70**:1153 (April 20) 1918.

2. Muckenfuss, R. S.; McCordock, H. A., and Harter, J. S.: Am. J. Path. **7**:552, 1931; **8**:63, 1932.

3. McCordock, H. A., and Muckenfuss, R. S.: Am. J. Path. **9**:221, 1933.

Fig. 1.—Interstitial bronchopneumonia from a case of whooping cough. Thickening and cellular infiltration of the bronchial wall as well as of some of the surrounding alveolar walls are noticeable. There is an exudate of polymorphonuclear leukocytes in the lumen of the bronchus and in a few of the adjacent alveoli.

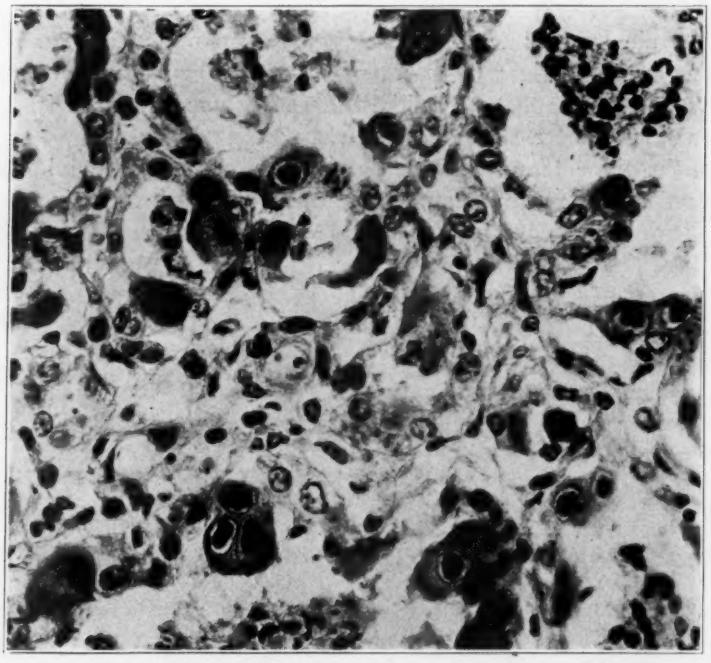

Fig. 2.—The intranuclear inclusions of whooping cough. Inclusions like a bird's eye can be seen in cells lining the alveoli and occasionally in detached cells free in the lumen.

mental work suggested that a virus might be necessary for the production of interstitial bronchopneumonia, and since this lesion is found in practically all fatal cases of whooping cough, it was necessary to seek evidence of the presence of such an agent in this disease. One of us [4] reported the finding of intranuclear inclusions (fig. 2) in the lungs of 12 of 35 children who had died of pertussis, and their absence in all but 2 of a control series of 90 autopsies. Since then new cases have brought our series to 40 autopsies, and 18 of these (or 45 per cent) have shown inclusions. The presence of cellular inclusions in such a high percentage of our cases of whooping cough is strong evidence of the possible association of a virus with this disease, because inclusion bodies are generally

Fig. 3.—One intranuclear inclusion can be seen in an epithelial cell lining a duct of the salivary gland from a child with no history of whooping cough. Groups of inflammatory cells can be seen on both sides of the duct.

regarded as having a specific relation to filtrable viruses. Feyrter,[5] in 1927, reported similar inclusions in a case of pertussis, and recently Rich [6] confirmed their presence by finding them in 4 of his cases.

When one of us [4] originally reported the finding of inclusions, it was stated that similar intranuclear inclusions had been found by a number of investigators in various organs in children with no history of whooping cough, and that Farber and Wolbach [7] had reported inclu-

4. McCordock, H. A.: Proc. Soc. Exper. Biol. & Med. **29**:1288, 1932.
5. Feyrter, F.: Frankfurt. Ztschr. f. Path. **35**:213, 1927.
6. Rich, A. R.: Bull. Johns Hopkins Hosp. **51**:5, 1932.
7. Farber, S., and Wolbach, S. B.: Am. J. Path. **8**:123, 1932.

sions in the salivary glands in 12 per cent of 183 autopsies on infants and young children. It was also stated that the salivary glands had not been studied except in 3 instances, in which, however, sections of the lungs either failed to show inclusions or contained only a few. In an attempt to determine the relation of the inclusions found in whooping cough to those observed in the salivary glands and other organs of children by earlier investigators, and recently studied by Farber and Wolbach,[7] we have examined the submaxillary glands found at autopsies on children since July 1, 1932. Salivary glands have been obtained from 6 children dying of postpertussis pneumonia between April and July 15, 1932. In 4 of these the salivary glands showed intranuclear inclusions. While only 3 of these showed inclusions in the lungs as well as in the salivary glands, the fourth disclosed inclusions in the salivary glands only, and these were found after prolonged search; in fact, on the basis of a preliminary examination the results were reported earlier as being negative.

In a group of 60 cases from the St. Louis Children's Hospital, which came to autopsy between July 1, 1932, and Feb. 7, 1933, in none of which the diagnosis was whooping cough, similar intranuclear inclusions were found in the salivary glands (fig. 3) 6 times. This incidence (about 10 per cent) is practically the same as that reported by Farber and Wolbach [7] (12 per cent of 183 autopsies) and by Löwenstein [8] (3 times in 30 autopsies). In association with the intranuclear bodies we have also observed the cytoplasmic inclusions mentioned by Farber and Wolbach.[7] We have seen these cytoplasmic inclusions in the lungs as well as in the salivary gland.

As yet the number of salivary glands obtained from cases of whooping cough is very small, but our observations suggest that the incidence of inclusions in the salivary glands in this disease is higher than in other conditions.

A further search has been made in both the current material and in material from former autopsies for inclusions of this type in the lungs and other organs of children dying of conditions other than whooping cough. In the 60 recent autopsies inclusions were found in organs other than the salivary glands only once and in the older autopsies (salivary glands not available) 7 times.

Although we have found these inclusions in a total of 14 children with no history of whooping cough, it may be emphasized that in only 8 of these were inclusions found in any organ other than the salivary gland. Seven of these 8 cases were obtained from a large number of autopsies on children during the past ten years, but, since sections from

8. Löwenstein, C.: Centralbl. f. allg. Path. u. path. Anat. **18**:513, 1907.

Inclusions Found at Autopsy on Children Dying of Other Conditions Than Whooping Cough

Date Age	Lung	Liver	Suprarenal Glands	Salivary Gland	Kidney	Clinical Data	Anatomic Observations
Group I: Pancreatic Fibrosis and Chronic Pneumonia							
December, 1927 4 months	+*	..	..	..	..	Wassermann reaction negative; cough for 1 month; convulsions; history of loose, green stools	Chronic pneumonia with peribronchial infiltration; pancreatic fibrosis and dilatation of ducts
August, 1932 5 months	..	..	..	+	..	Wassermann reaction negative; cough for 1 week; diarrhea since age of 2 weeks	Chronic pneumonia with peribronchial infiltration; pancreatic fibrosis and dilatation of ducts
December, 1932 3 months	+	+	+	..	+	Wassermann reaction negative; cough for several weeks; secondary pneumonia	Chronic pneumonia with peribronchial infiltration; pancreatic fibrosis and dilatation of ducts; foci of necrosis in liver and suprarenal glands
Group II: Chronic Pneumonia							
September, 1932 4½ months	+	..	..	..	..	Wassermann reaction negative; premature; malnutrition; rickets; secondary pneumonia; xerophthalmia; convulsions	Rickets; chronic pneumonia with peribronchial infiltration; focal infiltration in kidneys; no spirochetes
August, 1926 5 months	+	..	..	..	..	Cough for 2 weeks; secondary pneumonia; suppurative pleurisy	Chronic pneumonia and peribronchial infiltration; pulmonary abscesses; purulent pleurisy
July, 1926 2 years	+	..	..	..	..	Wassermann reaction negative; dysentery; cough for 2 weeks; gangrene of gums, palate and cheeks (noma)	Gangrene of face, gums, palate; chronic pneumonia with peribronchial infiltration; ulcerative colitis
August, 1931 3 months	+	..	..	..	..	Wassermann reaction negative; cleft palate; otitis media; secondary pneumonia	Cleft palate; chronic pneumonia with peribronchial infiltration
January, 1933 4 months	..	..	..	+	..	Wassermann reaction positive; premature; cough for 1 week; secondary pneumonia	Chronic pneumonia with marked peribronchial infiltration; syphilitic osteochondritis; fibrosis of myocardium
January, 1933 18 months	..	..	..	+	..	Wassermann reaction negative; erysipelas; multiple abscesses	Chronic pneumonia with peribronchial infiltration; no abscesses in lungs
Group III: Various Unrelated Lesions							
December, 1929 1 day	+	..	..	..	..	Wassermann reaction negative; jaundice; multiple hemorrhages	Blood formation in spleen and liver; slight pancreatic fibrosis; focal infiltration in kidney; no spirochetes
May, 1932 6 months	..	+ few	..	..	..	Drowsiness; periods of muscular rigidity; bloody spinal fluid	Hemorrhage from cerebral vessel, no explanation; no spirochetes
October, 1932 4 months	..	..	..	+	..	Wassermann reaction negative; cough for 2 weeks; otitis media; secondary pneumonia	Slight peribronchial infiltration; acute pneumonia
December, 1932 13 years	..	..	..	+	..	Osteomyelitis; multiple abscesses	Osteomyelitis; abscesses; septicemia; no lesion in lungs
January, 1933 6 months	..	..	..	+	..	Symptoms of severe acute infection of unknown character	No lesions to account for symptoms or death

* Inclusion bodies are present.

only a portion of the total number of autopsies performed during this decade were examined, no idea of the frequency of these inclusions in cases which came to autopsy during that period can be obtained. However, in the new series of 60 autopsies since July 1, 1932, inclusions were found in organs other than the salivary glands only once, and in this instance no inclusions were seen in the salivary glands. In the material from former autopsies, salivary glands are not now available, but in the recent autopsies they are included as a matter of routine.

The table demonstrates the character of the conditions other than whooping cough with which the intranuclear inclusions were associated.

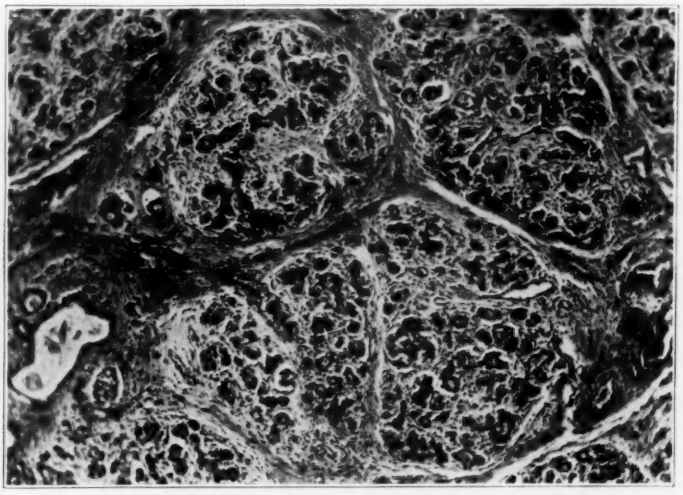

Fig. 4.—Fibrosis of the pancreas from a child with no history of whooping cough. In this case there was also chronic pneumonia, and intranuclear inclusions were found in the lungs and salivary glands.

The 3 autopsies which showed chronic pneumonia with peribronchial mononuclear cell infiltration and marked pancreatic fibrosis (fig. 4) with dilatation of the ducts are of interest because of the striking similarity in the clinical and anatomic findings in these cases. A review of the literature reveals the occurrence of this pancreatic lesion in a number of cases in which similar intranuclear inclusions were found in various organs. Future observations may show that the fibrosis of the pancreas associated with intranuclear inclusions in the salivary glands and occasionally in other organs may represent some as yet unrecognized disease entity, caused perhaps by the filtrable virus responsible for the inclusions under discussion. There was no question of congenital syphilis in any of the children in this group in our series.

Congenital syphilis was definitely present only once in our 14 cases, although its existence was suspected in a considerable number of similar cases in the literature. One wonders to what extent fibrosis of the pancreas, a frequent lesion in congenital syphilis, may have influenced earlier authors in making a presumptive diagnosis of syphilis when definite serologic evidence and the demonstration of the spirochetes were lacking.

The frequent occurrence of pneumonia with a marked peribronchial infiltration of mononuclear cells resembling that seen in whooping cough is another point of interest, brought out in the table.

The significance of the intranuclear inclusions so frequently associated with whooping cough and their relation to those occasionally found in a variety of other conditions is open to several possible interpretations.

1. In whooping cough the inclusions may be due to the activation of a latent endogenous virus or to a virus which enters the lung as a secondary invader during the course of the disease. These possibilities, however, fail to explain why such a virus does not complicate a large percentage of other chronic pulmonary infections in children. Such a possibility was recently expressed by Rich [6] who suggested that the virus in question may be that of herpes which is aspirated during the course of the disease. However, morphologically the inclusions observed in whooping cough are not identical with those of herpes, and we have never succeeded in producing in rabbits the lesions of ocular herpes or of encephalitis with ground up human tissue containing inclusions.

2. Another possible interpretation is that in those cases in which inclusions are demonstrated, the condition diagnosed as whooping cough might be regarded as a distinct disease entity caused by a virus, and confused clinically with another group of cases presenting similar symptoms but due to the pertussis bacillus. This view is difficult to uphold because a large percentage of our cases with inclusions have shown the blood picture believed to be characteristic of whooping cough by those who regard the Bordet-Gengou bacillus as the only cause of the disease. Also, the anatomic lesions in the lungs are identical whether inclusions are present or not.

3. The inclusions found in whooping cough and in other conditions, although morphologically identical, may represent the action of more than one virus. The striking similarity of the lesions in the group of those cases in which the pancreas is involved suggests that these may represent infection by a distinct virus. The existence of morphologically similar inclusions in the salivary glands of guinea-pigs suggests that a related virus may be the cause of the inclusions in the salivary glands in children. They are not caused by the same virus, however, because

we have been unable to transmit the condition by means of inoculation of young guinea-pigs with infected tissue from children. If the inclusions occurring in different conditions are due to different viruses, then those found in whooping cough may be considered as in all probability caused by a "pertussis virus." It is, however, unlikely that we have to deal with a large number of different viruses in children all producing identical inclusions.

4. All of the intranuclear inclusions that have been observed in children may be the result of the presence of a single virus. If this is true, the fact that the virus in question is so frequently associated with whooping cough, and so seldom with other conditions, would permit one to regard it as having a specific relation to this disease. According to this interpretation the virus associated with whooping cough would also be the cause of the inclusions occurring in other unrelated conditions, and the children showing them might be looked on as carriers or as those in whom no clinical signs of the disease had been detected.

We have shown that interstitial bronchopneumonia, which so frequently complicates whooping cough, can be reproduced in animals by the combined action of a virus and bacteria. Furthermore, the work of Schope [9] on swine influenza indicates that a specific relationship may exist between a certain virus and a particular bacterium which constitute the two etiologic components of that disease. He showed that although the virus alone produces a mild "filtrate disease" and that the bacterium (Haemophilus influenzae-suis) by itself is without effect, the combined action of these two etiologic elements produces the typical influenza of swine. In a similar manner, it is possible that children with no history of whooping cough who show intranuclear inclusions in various organs with or without an interstitial infiltration in the lungs may be suffering from a mild virus disease which is of little consequence unless a simultaneous or a secondary bacterial infection complicates the condition. The accumulated evidence of past work definitely associates the Bordet-Gengou bacillus with the clinical disease known as whooping cough. It is possible, therefore, that this organism represents the usual bacteriologic component in a hypothetical virus bacteria complex necessary for the production of the interstitial bronchopneumonia complicating whooping cough and perhaps also for the clinical manifestations of this disease. That other related respiratory bacteria can at times replace the Bordet-Gengou bacillus in this complex would then be indicated from the report of Brown [10] who showed that Bacillus bronchisepticus and not the Bordet-Gengou bacillus was present in a typical case of whooping cough.

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9. Schope, R. E.: J. Exper. Med. **54**:349 and 373, 1931
10. Brown, J. H.: Bull. Johns Hopkins Hosp. **38**:147, 1926.

Which of these four possibilities is correct cannot definitely be decided from the evidence now available. The intranuclear inclusions in the lung in cases of whooping cough and of other diseases and those in the salivary glands appear morphologically identical. Until these inclusions can be reproduced experimentally the relation between those found in a high percentage of children dying of pertussis and those observed in a much smaller percentage of children dying of a variety of other conditions cannot definitely be determined. An anatomic and statistical study cannot give the final answer to such a question.

FREQUENCY OF PYURIA IN ANOMALIES OF THE URINARY TRACT IN CHILDREN

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MATERIAL FOR STUDY

To determine how often infection with pyuria occurs in the presence of congenital anomalies and acquired obstructive lesions of the urinary tract eighty-five children with ninety-nine such lesions have been studied. The children have been divided into two groups depending on whether or not pyuria was present. Such a comparative study brings out the following points of clinical interest: (1) the relation of infection to urinary stasis; (2) the relative frequency of congenital anomalies of the urinary tract as compared to the acquired ones; (3) the frequency with which pyuria occurs when such lesions are present; (4) the age at which anomalies of the urinary tract are usually recognized—although the great majority of them are congenital; (5) the relation of diagnosis to the presence of symptoms, pyuria and the findings on physical examination; (6) the large number of anomalies which will not be diagnosed because suspicion of their presence is not aroused owing to the absence of symptoms and positive findings on physical examination.

Although there have been many reports in the literature on anomalies of the urinary tract, they have dealt mostly with the types and the frequency of occurrence or only with the lesions accompained by infection.

For want of a better word, the general term "anomaly" is used in this article to include not only congenital abnormalities but also acquired ones. Cases of pyuria, often called cystitis or pyelitis, not accompanied by some other anatomic abnormality of the urinary system as well as all cases belonging to the group with nephritis are excluded. The patients in each group are divided according to age and according to the type of anomaly. As stated, eighty-five children with ninety-nine anomalies of the urinary tract, all patients in the Children's Memorial Hospital, are included in this study. There is no service for the new-born at the hospital, but infants and children up to 13 years are admitted. The cases included comprise all the anomalies encountered during the past five years with the addition of a few seen earlier. It might be well to add that because of the frequent discovery at necropsy of undiagnosed

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anomalies of the urinary tract an especially careful watch for these cases has been kept during the past five years.

The cases have been gathered from both clinical and postmortem sources. Of the clinical cases attention was directed to the possibility of an anomaly of the urinary tract in most patients by the presence of a chronic pyuria. This is the symptom that usually brings these children to the physician. A smaller number of clinical cases without pyuria were recognized because of an abdominal tumor mass, dysuria, dribbling or enuresis. In contrast, at postmortem examination most of the urinary anomalies were chance findings, and comparatively few of these were accompanied by a pyuria.

Accurate percentages of the frequency with which pyuria occurs are not available, while the incidence of anomalies of the urinary tract is based on either clinical or postmortem studies. That many anomalies remain unrecognized is deduced from the number found unexpectedly

TABLE 1.—*Anomalies of the Urinary Tract with Pyuria*

	Number of Cases	Aged Under 1 Year	Aged from 1 Year to 5 Years	Aged from 5 Years to 13 Years
Hydronephrosis	19	7	4	8
Reduplication of ureter or pelvis (4 with hydronephrosis)	5	3	0	2
Obstruction of the neck of the bladder	7	3	2	2
Cord bladder	1	..	1	..
Calculi in the urinary tract	5	..	..	5
Ptosis of the kidney	1	..	..	1

at necropsy in patients whose death was due to some unrelated cause or to a terminal renal infection. That congenital anomalies of the urinary tract are common has been brought out in several reports of necropsy series in which the incidence has varied from 1.3 to 12 per cent. This high percentage reveals the importance of the urinary system in relation to disease morbidity in infancy and childhood. This is of special significance since only about half of these lesions are associated with the general symptoms of infection and pyuria, or with local symptoms and findings on physical examination that might direct attention to their presence.

ANOMALIES OF THE URINARY TRACT WITH PYURIA

In table 1 are grouped thirty-eight anomalies found in thirty-two children who had a pyuria. In fifteen of the nineteen cases of hydronephrosis, the hydronephrosis was the only lesion present. In six of these the pelvis of the kidney alone was dilated, one bilaterally and five unilaterally, and in nine there was a dilatation of both ureter and renal pelvis, four bilateral and five unilateral. The obstruction was either at the ureteropelvic junction or in the ureterovesical region in all

but two cases. In one of these, there was a nonpatent pelvis with cystic sacculation of the kidney, while in the other no obstruction was found in the urinary tract although there was a marked dilatation and thickening of the ureters and pelves. This last child reported on was a boy 8½ years of age, who died with a clinical diagnosis of postdiphtheritic paralysis and uremia. The hydronephrosis was an unexpected finding at necropsy. This is the only child in whom hydronephrosis was present without demonstrable obstruction. On microscopic examination there was a generalized inflammatory hyperplasia of the walls of the ureters and pelves. It is the only case in which it could possibly be thought that infection preceded or had anything to do with the hydronephrosis. In nine cases the hydronephrosis was recognized clinically and was treated by the urologist. In six it was a chance finding at necropsy, although in three of these the pyuria was discovered ante mortem, but owing to the critical condition of the children (they died shortly after coming under observation) urologic examination was not thought necessary, practical or of any value at this stage of the illness. In two children the pyuria was due to a terminal renal infection which seemed to have no relation to the hydronephrosis, i. e., the pyonephritis developed in the course of a septicemia. In addition to the aforementioned fifteen cases there were four cases of hydronephrosis with reduplication of ureters and seven with obstruction of the neck of the bladder which brings the total to twenty-six.

There were five patients with reduplication of the pelvis or ureter. Of these, four had a hydronephrosis which was recognized and clinically treated in two and found at necropsy in the other two. In the fifth case there was no hydronephrosis, and the pyuria was due to a terminal infection of the kidneys from septicemia.

Seven patients with obstruction of the vesical neck had a pyuria when they first came under observation. In one child (10 years of age) obstruction was due to a prostatic abscess; in three (aged 4, 5½ and 9 years, respectively) the obstruction was due to urethral valves, and in the other child (1 year of age) a urethral stricture, of undetermined type, was diagnosed. This last child and two with bar obstructions were operated on by the urologist and are getting along well clinically. Only in the two infants with the urethral valves and in the 4 year old child with a bar obstruction was the anomaly a chance finding at necropsy. Eight other cases of obstruction of the vesical neck will be considered in the group without pyuria although in five of them, after the condition had been recognized clinically, a pyuria developed following urologic investigation. The other three cases were first recognized at necropsy as no urologic investigation had been carried on. Another child with a large hydronephrosis of the right kidney had no pyuria when first seen; but immediately after ureteral catheterization

pyuria developed on that side. In cases with obstruction and urinary stasis, infection and pyuria, when not previously present, invariably followed cystoscopy or catheterization. Although it has been known from ancient times that this happens, it is often not kept in mind when catheterization is being considered.

In one instance a definite ptosis of the kidney was found on urologic examination. This child, aged 9 years, was examined because of the presence of a marked pyuria. At necropsy there were, besides the ptosis, bilateral abscesses of the kidney, endocarditis, and septicemia.

Two patients had renal pelvic calculi, one with a ureteral calculus, and two with calculi in the urinary bladder. All the conditions were recognized clinically. Two of these children had obstructions of the vesical neck.

TABLE 2.—*Anomalies of the Urinary Tract Without Pyuria*

	Number of Cases	Aged Under 1 Year	Aged from 1 Year to 5 Years	Aged from 5 Years to 13 Years
Hydronephrosis	16	8	6	2
Reduplication of the pelvis or ureter	12	8	1	3
Obstruction of the neck of the bladder	8	3	2	3
Absence or hypoplasia of the kidney	4	3	1	..
Horseshoe kidneys	5	2	2	1
Exstrophy of the bladder	2	1	..	1
Prolapse of the urethra	1	..	..	1
Urethral stricture	1	..	..	1
Calculi in the urinary tract	3	1	1	1
Tumors (5 with hydronephrosis)	9	2	7	..

ANOMALIES OF THE URINARY TRACT WITHOUT PYURIA

In table 2 are grouped sixty-one anomalies found in fifty-three children who did not have pyuria. It will be noted that there are more younger children in this group than in that of table 1. Most of these lesions were found post mortem rather than clinically.

Of eleven of the patients with hydronephrosis, in five the obstruction was at the pelvo-ureteral junction, and in five, in the ureterovesical area; one had a ureteral valve. In only one of these eleven children was the lesion recognized ante mortem. This sounds like poor clinical diagnosis, but such was really not the case. In the patients with the unrecognized lesions there was no pyuria with its symptoms of infection, no palpable abdominal tumor mass, and nothing in the clinical history or in the physical examination led the examiner to suppose that a lesion of the urinary tract was present. The child in whom the lesion was recognized was a boy 18 months of age who was brought to the hospital because of a large abdomen. On urologic investigation a large hydronephrosis of the right kidney was found. Repeated examinations of the urine before cystoscopy gave negative results but immediately after ureteral

catheterization a pyuria developed only on the obstructed side, as proved by further cystoscopic examinations. The pyuria persisted until removal of the hydronephrotic kidney. In five other children a hydronephrosis associated with a kidney or retroperitoneal tumor was present. Adding the eight cases of hydronephrosis with obstruction of the neck of the bladder gives a total of twenty-four children with hydronephrosis and stasis without pyuria.

Of the eight children with obstruction of the neck of the bladder the condition was recognized clinically in five (aged 4 days, 2 months, 18 months, 8½ years and 9 years) and in three (aged 5 months, 1 year and 12 years) it was found only at necropsy. In the five children in whom the anomaly was recognized clinically a pyuria developed after urologic investigation. Of these five, two were operated on, one recovered and one died. In three of the eight children the obstruction was due to urethral valves and in three, to bars at the vesical neck. One other had obstruction (type not stated) in the posterior urethra, and in one the type and exact location of the obstruction were not stated. There were also two patients who had temporary obstruction of the neck of the bladder with enormous dilatation of the bladder due to tumor masses, which proved to be chordomas. Both were diagnosed clinically, and no pyuria was present.

Twelve children had a reduplication of the pelvis or ureter. Eleven of these were chance findings at necropsy, there being no clinical symptoms or physical findings to denote their presence before death. The one child in whom the condition was recognized clinically was a girl 10 years of age who had had constant dribbling since birth. On urologic investigation the extra-ureteral opening was found distal to the vesical sphincter. The reduplication was unilateral in ten children and bilateral in only two. There was a pair of male twins with exactly the same type of reduplication. In one child with a reduplication of the pelvis there was also a large tumor of the kidney on the same side.

An absence of one kidney, discovered only at necropsy, occurred in two instances. In each of two children with obstruction of the neck of the bladder there was a marked hypoplasia of one kidney, the hypoplastic kidneys being bean-sized. In both cases there were nonpatent ureters on the sides of the hypoplastic kidneys.

Five children had horseshoe kidneys, discovered only at necropsy. In one there was an associated obstruction of the neck of the bladder with hydronephrosis. In two, fusion was at the lower poles, and in three at the upper poles.

Exstrophy of the bladder was present in two children. One child, who was seen at 2½ years of age and followed at irregular intervals, did not have pyuria at any time as shown by ureteral catheterization. As urinary stasis was not present, pyuria did not develop after catheteriza-

tion. When the boy was aged 12 years, one ureter was resected and transplanted into the bowel; a few months later the other ureter was similarly transplanted, and a few months later the remnant of the bladder was resected. Within three months after each ureteral transplantation a large hydronephrosis developed on the same side. Whether this was due to ureteral obstruction in the wall of the bowel or to infection cannot be stated, but the former would seem to be the more logical assumption. The other child died at 5½ months of age. There was no pus in the urine obtained by ureteral catheterization, although there were ulcerations of the exposed bladder and infection about the ureteral openings. No other infection of the urinary tract was found at autopsy.

One child, a girl, had a prolapse of the urethra which had been present for over a year. Another child, a boy, had a stricture of the

TABLE 3.—*Anomalies of the Urinary Tract With and Without Pyuria*

	Number of Cases	With Pyuria Recognized		Without Pyuria Recognized	
		Ante Mortem	Only at Necropsy	Ante Mortem	Only at Necropsy
Hydronephrosis	35	11	8	1	15
Reduplication of ureter or pelvis	17	2	3	1	11
Obstruction of the neck of the bladder	15	4	3	5	3
Calculi in the urinary tract	8	5	..	1	2
Absence or hypoplasia of the kidney	4	..	..	..	4
Horseshoe kidneys	5	..	..	..	5
Cord bladder	1	1	..	..	..
Exstrophy of the bladder	2	..	..	2	..
Ptosis of the kidney	1	1	..	..	..
Tumors	9	..	..	9	..
Prolapse of the urethra	1	..	..	1	..
Urethral stricture	1	..	..	1	..

urethra with three small urethral fistulas proximal to the stricture; this had been produced three years previously when a string had been tied around the penis by another boy.

Calculi in the urinary tract without pyuria were found in three children. In two of these patients, 1 and 3 years of age, the pelvic calculi were small and were found only at necropsy. In the third child, a girl 12 years of age, only red blood cells, but never evidence of pyuria, were found on repeated examinations of the urine. On urologic examination a stone was discovered in the pelvis of one kidney.

Three patients had primary tumors of the kidney. Two were Wilm's tumors, with, in one case, an obstruction of a ureter due to a metastatic growth. One child with bilateral polycystic kidneys had a superimposed bilateral cyst-adenocarcinoma. There were six children with retroperitoneal tumors, including two lymphosarcomas, one round cell sarcoma and one actinomycotic mass of glands, all of which caused marked pressure on the kidneys and ureters with moderate urinary stasis. Two of the tumors were chordomas, one of the true pelvis and the other invading

the wall of the bladder. Both of the chordomas caused sufficient pressure on the bladder to produce marked urinary retention, and catheterization was necessary for some time. In five of the aforementioned nine cases a moderate hydronephrosis was present.

In table 3, for comparison, the cases are classified according to lesions and the presence or absence of pyuria. The lesions recognized clinically and those recognized only at necropsy are indicated in each group. It can be seen that about half of the children had pyuria.

COMMENT

The great majority of lesions with obstruction were of the congenital type, only a few being due to pressure from without the urinary tract. In no instance was it clearly indicated that infection was the cause of the obstruction. The usual sites of obstruction were at the pelvo-ureteral junction, in the ureterovesical area, at the neck of the bladder or at the distal end of an anomalous ureter.

In one child 4 days of age with an obstruction of the neck of the bladder a nonpatent ureter was found with a hydronephrosis on the same side. The ureter was completely occluded at the point of entrance into a diverticulum of the bladder. In another child 6 weeks of age one ureter was of small caliber but patent, the pelvis of the kidney was empty, and there were large sacculations of the kidney with a complete absence of kidney substance due undoubtedly to atrophy caused by pressure. It seems that in both of these children renal secretion must have been present before birth.

All the obstructions of the neck of the bladder in this series, both those found clinically and at necropsy, occurred in boys. Six of these were diagnosed as bar obstructions of the neck of the bladder by the attending urologist, Dr. H. L. Kretschmer. In these six there was no obstruction in the posterior urethra. At the neck of the bladder a definite ridge was found which projected upward just inside of the urethral opening thereby partially occluding it and causing a definite obstruction to the outflow of urine from the bladder. There was dilatation and hypertrophy of the bladder and marked dilatation of the ureters and pelves. It does not seem possible that the hypertrophy of muscle causing the bar could be a secondary change due to some other undiscovered lesion in the urethra or bladder.

There was a definite difference in the ages at which the posterior urethral valve obstructions and the obstructions of the neck of the bladder were found. The cases of urethral valves were all in children under 1 year of age while the bar obstruction occurred in older children, only one case being found in a child under 1 year of age. This seems to indicate that the valve obstructions are all rather marked from early

infancy, while obstructions due to bars in the vesical neck are not so severe in early life but increase as the child grows older. Because of the definiteness of the obstruction, in the absence of signs of an inflammatory reaction and of scar tissue, the bars have all been considered to be congenital. Microscopic examination of the tissue of the bars showed essentially only hypertrophy of the muscle. The explanation of this hypertrophy is not easy, just as the mechanism of the obstruction at the ureteropelvic junction or in the ureterovesical region is not clear. The lesions are considered to be congenital because they are found during early infancy. Whether the initial abnormality is one of muscular tissue or of neurogenic function is not known. It is noteworthy, too, that all the obstructions of the neck of the bladder occurred in boys.

SUMMARY

To determine the frequency of infection of the urinary tract with pyuria in congenital anomalies of the urinary tract and acquired obstructive lesions eighty-five children with ninety-nine such lesions have been studied. Of these eighty-five children, thirty-two had pyuria. In sixty-nine of the children the lesion was considered to be congenital. Urinary stasis due to obstruction somewhere in the urinary tract was present in fifty-two instances. In these the lesion was congenital in forty-five. Of the fifty-two cases with obstruction, pyuria was present in only twenty-six. Of thirty-six children in whom the lesion was recognized during life there was obstruction with urinary stasis in twenty-four and pyuria in twenty. The lesion was a chance finding at necropsy in forty-nine instances, although in twelve there was pyuria and in twenty-eight, obstruction with urinary stasis. Death could be attributed directly to the pathologic process of the urinary tract in sixteen cases, and it undoubtedly had some influence in the death of some of the other children.

CONCLUSIONS

1. Anomalies of the urinary tract are of frequent occurrence, and the majority of them are congenital. In this series, so far as could be determined, none of the urinary obstructive lesions were due to acquired stricture caused by infection or inflammatory reaction in the ureteral wall.

2. Many such lesions go unrecognized for a number of years because of the lack of recognizable symptoms.

3. Obstructive lesions with urinary stasis may be present for years without infection and pyuria.

4. Since 50 per cent of the children with urinary stasis had pyuria, it appears that urinary infection in these children may be more frequent than in normal children, but that stasis, contrary to the usual belief,

does not always lead to pyuria. When infection does take place it is exceedingly persistent, even becoming permanent, unless the obstruction is relieved.

5. Catheterization or the manipulations of urologic investigation invariably lead to infection when stasis is present.

6. A normal urine does not exclude the possibility of an obstructive lesion of the urinary tract.

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SELECTION OF MALNOURISHED SCHOOL CHILDREN

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Methods of selection of physical defects among school children have a far-reaching influence on the school health service as a whole. They must be practical and economical, of course, but that is only one way in which they affect the total efficiency. They also have an important bearing on the way the child is viewed by the school medical examiner to whom he is referred and on the type of information that the school nurse takes with her on the follow-up visit. How many of the children who are 7 per cent underweight for height are truly malnourished and how many of those examined are missed by this method? This query involves two sources of inefficiency—selection in error and failure to detect.

Such error of selection has a profound influence on the obligation of the school medical examiner to explain the case and prescribe further study. If the child is referred back from the medical examiner with no explanation (as is the case with the height-weight method), obviously an unproductive reference method has been developed. On the other hand, if the teachers are reasonably accurate in their selection, the school medical examiners to whom such cases are referred may concentrate their attention on the underlying reasons for the condition. From such careful consideration they may properly advise the school as to what further steps to take. The submission of real cases to physicians would obligate them to decide whether or not the circumstances warrant the school in going to the trouble and expense of notifying parents and sending nurses to homes to advise that medical consultation be sought.

The method of selection extends its influence even further. If the physician is so impressed by the authenticity of the cases referred to him that he feels obliged to make a definite decision as to the school's further responsibility, the nurse has a real authoritative basis for counseling the parents. If the original selection is poor, and the physician waives any decision in the case, the nurse must either ignore the case or proceed on her follow-up with no other authoritative basis

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This article covers the main points which Dr. Franzen presented in a talk entitled "Some Outcomes from a Study of the Effects of School Health Programs on Children" before the Child Hygiene Section at the last annual meeting of the American Public Health Association.

than the admittedly inadequate original selection. There is little point in following up such cases when an authoritative professional opinion is lacking. If the nurse is to accomplish anything in the home, she must be armed with real important facts about the individual child. It is not economical to go through this entire routine, starting with the original selection, if all that the nurse can transmit to the parents of children thus laboriously selected is some general information that possibly the child's dietary or living habits are at fault.

One should be able to find most of the cases of malnutrition by some practicable economical measure, refer them to medical examination with a definite obligation to provide the decision as to whether further attention is necessary and, if so, proceed with a follow-up that has a conscious, authoritative direction. These are the three dominant qualities of an efficient school program for the correction of defects. And they all depend on the original method of measurement used to mark children for further consideration.

A number of proposals have been made for selecting malnourished children by the extensive application of a simple examination. The best known example is the device known as percentage underweight for height. Most of the devices are rational rather than empirical in origin; that is, they have been based on considerations of what, for a priori reasons, seemed serviceable rather than on evidence that the objective sought was really being attained. Efficiency demands that whatever method is used must in its essentials be a truthful estimate of nutritional status.

RATIONAL FORMULAS

The distinction between a rational formula and an empirical one is not in the amount of measurements available. It arises directly in the question whether the evidence was used to derive the formula or to arrive at standards in its application. There is a great deal of accumulated material on relationships of height to weight, but none of it has been employed to substantiate the method or to find its true meaning. The only use to which the evidence has been put is to arrive at standards. It is a rational formula. This is true of the Pirquet and the Pelidisi formulas. It is also true of such formulas as:

$$\frac{\text{Chest Circumference} \times \text{Upper Arm Girth}}{\text{Height}}$$

They are not built from experimental evidence, and consequently they have no analytic foundation.

EMPIRICAL FORMULAS

In contrast to such rationalized measures stands the empirical method. It employs evidence to derive its formulas. Assumptions

must be made, of course, but conclusions are reached in terms of the assumptions. For instance, the following basic assumptions can be made: 1. The condition of the muscles and subcutaneous tissue is an index of nutritional status. 2. Individual differences in weight, muscle and subcutaneous tissue are relevant only when skeletal differences are excluded.

The defense of the wisdom of these assumptions lies in the experience and judgment of members of the medical profession. It may be experimentally shown that physicians attempt to estimate muscle and adipose tissue when they rate a child for nutrition, that they fail to agree on the condition of the child because their estimates of these qualities do not agree and that complete agreement ensues from a common consideration of objective measured evidence of these qualities. Reference made when these factors have been measured always implies the obligation to explain their causes. It may also be shown that physicians allow for skeletal build when they are supplied with evidence that makes such allowance possible. The reason for this is their desire to distinguish immediate influences on weight and muscle from those that are more remote. Professional estimates of malnutrition aim at immediate histories of diet and food and not at endogenous causes.

Theoretical consideration of these assumptions and the empirical derivation of measures based on them appears elsewhere.[1] It will suffice here to note that such formulas are not a simple mathematical proposal, but rather the best derived statistical statement of the problem as defined. They are the end-results of mathematical experimentation.

These formulas are too elaborate for practical application, but they serve as an entirely satisfactory standard against which to judge abbreviated methods which are being considered for actual use. By comparing any given method with this standard one may determine how many cases each method misses and how many it selects in error. This knowledge will assist school administrators in determining their own course of procedure.

THE METHOD OF EVALUATION

For the purposes of this paper it is assumed that when a child is markedly below his skeletal peers in weight, amount of muscle and amount of subcutaneous tisssue, he may be called malnourished, and that a follow-up procedure in regard to him is a good public health investment. Time and money are not available to survey all children in a school system with the full elaboration of measurement and so sort out those who show such deficiency. Short cuts are necessary. The one that best achieves the purpose is the one that discovers most of those sought and selects the least in error.

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1. Franzen, R.: Physical Measures of Growth and Nutrition, New York, American Child Health Association, 1929, monograph no. 2.

It would be helpful, then, to find a practical preliminary screening procedure. Simple, easily applied measurement of all children could be followed by intensive consideration of a selected few. But most important from the standpoint of economy of administration is that the pupils most in need of attention be correctly selected. The immediate problem, therefore, is what extensive measurement should be made with the expectation that intensive consideration will follow for those who are selected by the more readily applicable index.

THE EVALUATION

Five hundred children 11 years of age (250 of each sex) were exposed to an intensive anthropometric survey. They were measured for weight, five skeletal traits, the amount of subcutaneous tissue in three areas and the amount of muscle in the upper arm, calf and deltoid areas. With these materials it was possible to apply formulas derived in the course of the School Health Study of the American Child Health Association, and to select extreme deviation in weight, amount of subcutaneous tissue and amount of muscle. Critical deviation was defined statistically in such a way that about the lowest fifth of a normal sampling was achieved. The same criterion could be set to select about one tenth, or any other proportion instead of one fifth, without changing the conclusions in regard to the relative merit of the primary selective devices.

Four preliminary methods of selection were compared as to their efficacy in picking out cases of extreme deviation in terms of the criteria mentioned. They are: (1) weight for height; (2) weight for height and width of hips; (3) arm girth, chest depth, hip width screen (which for simplicity will be referred to hereafter as the A. C. H. screen),[2] and (4) rating by a medical examiner. The Baldwin-Wood tables were used to compute the percentage under weight. The height-hip-weight indexes were computed by the use of a regression equation obtained from a large random sampling, and these indexes must yield fully as much if not more than those used by Lucas and his co-workers.[3] Therefore the value of any simplified use of these three variables is no greater than the regression that is being evaluated here. The A. C. H. screen is explained by the score card reproduced. Ratings by the medical examiner were made on the Dunfermline scale in which 1 is good and 4 is

2. This was developed from School Health Study data for application in connection with the School Medical Examination Study now in progress in the city of New York, which is being supported by the Metropolitan Life Insurance Company. *A* stands for arm girth, *C*, for chest depth and *H*, for width of hips.

3. Lucas, W. P., and others: J. Pediat. **1**:572 (Nov.) 1932.

poor or very poor. Children who are rated as 4 by any one of six physicians were selected.[4]

SCORE CARD I (ELEVEN-YEAR-OLDS)

Name .....

School..... Room..... Grade.....

Sex..... Date..... Address.....

MEASUREMENTS

Flexed a .....

Arm Girth.....

Relaxed b ..... c.....

Inspiration d .....

Chest Depth.....

Expiration e ..... f.....

Width of Hips g.....

Difference Arm Girth—Chest Depth.....

CRITERION FOR SELECTION

Width of Hips	Minimum Difference Between Arm Girth and Chest Depth
21—21.9	4
22—22.9	4
23—23.9	5
24—24.9	6
25—25.9	6
26—26.9	7
27—27.9	8
28—28.9	9
29—29.9	10
30—30.9	11

DIRECTIONS

1. Add the two arm girth measures.
2. Add the two chest depth measures.
3. Subtract the latter from the former.
4. If this difference is less than the amount allowed on the table for the width of the hips, the child is selected.

4. The material used in the case of physicians' ratings was not the same as the rest. The source of these data was 100 boys 11 years old.

The three methods of measurement are all practical in school situations. The time of measurement is a little longer with the A. C. H. screen, but there is no computation or reference to tables in making the selections except that which is included on the scoring card. One person can apply this screen to 150 children in a school day.

The best way to use any of the three methods is as a screen to select the children who need to be measured more thoroughly. It would be helpful to have a test which would screen about 1 of 5 to receive the more thorough examination. The value of this test may be judged by its inclusion of children who show malnutrition when the complete examination is applied. It is not intended in the preliminary test to pick only such cases, but most of them must be included among the screened cases.

First, one should see what the various selective methods will do in picking out children who are markedly below the weight to be expected in consideration of their skeletal build. This means not just weight for height, but weight for four skeletal dimensions. Among the 250 boys, 52 were critically below the weight expected from their skeletal build (table 1). The first preliminary selective method, weight-for-height, yields only 23 of these true "weight deviates" (those underweight for skeletal build). That is, when the percentage underweight for height is set to net the lowest 52, only 23 of the true weight deviates are included. This corresponds to the number that are 7 per cent or more below average weight for height.[5] Thus by using the weight-height-age tables one would get less than half of the boys who really are underweight for their skeletal build in the degree already described. The difference between 23 and 52, or 29, represents the number of true weight deviates that are missed; and it also represents the 29 children who are selected in error. They are picked by the weight-for-height method, but are not really deficient in weight when a more complete estimate of skeletal build is considered.

Selection of the 52 children who are farthest below the weight expected for their height and hips yields only 27 of the true weight deviates. The A. C. H. screen method applied in the same manner yielded 30 of the true weight deviates. The ratings of individual medical examiners yielded 16.

These results are strictly comparable, since the worst 52 cases of the total group were selected for each test. The data are given in table 1, which also shows similar findings for girls. The weight-for-height method is even less successful in the case of girls.

5. It is about 10 per cent or more below the average for girls. Incidentally, this shows that if weight for height is used, the line of demarcation should be different for the two sexes.

An interesting conclusion is that the A. C. H. screen method nets the best yield and yet this method does not use weight in its formula. It is based wholly on arm girth, chest depth and width of hips.

If the objective is merely to find children who are underweight for their skeletal build, then the height-hip-weight method and the A. C. H. screen are about equally successful. Even these miss nearly half the

TABLE 1.—*Comparison of Devices for Selection with True Deviation in Weight as the Criterion*

Device: Weight with Allowance for Skeleton	Number of Boys 52	Number of Girls 50
Height-weight	23	15
Height-hip-weight	27	23
A. C. H. screen	30	26
Rating by medical examiner*	16	

* Lowest possible rating by any one of six physicians making independent judgments. Figures for girls are not available.

TABLE 2.—*Comparison of Devices for Selection with True Muscular Deviation as the Criterion*

Device: Amount of Muscle with Allowance for Skeleton	Number of Boys 50	Number of Girls 56
Height-weight	20	19
Height-hip-weight	22	25
A. C. H. screen	34	43
Rating by medical examiner	13	

TABLE 3.—*Comparison of Devices for Selection with True Deviation in Subcutaneous Tissue as the Criterion*

Device: Amount of Subcutaneous Tissue with Allowance for Skeleton	Number of Boys 55	Number of Girls 73*
Height-weight	15	28
Height-hip-weight	24	29
A. C. H. screen	28	37
Rating by medical examiner	14	

* This number goes up because of a positive skewness in the distribution of the quality for girls.

cases. The height-weight method, however, misses two thirds of the cases. Estimates of true deviation in weight are very inadequate unless at least two skeletal dimensions are used.

The objectives do, however, include more than weight. Suppose it is desired to pick out children who are below the musculature which is normal for skeletal build. Table 2 gives the numbers chosen by each of the four selective methods. Among 50 boys lowest in musculature among the 250, the weight-for-height method picked 20, the height-hip-weight method 22, the A. C. H. screen 34 and the rating by the medical

examiner 13. The A. C. H. screen is distinctly superior for this purpose. The screen yielded 70 per cent of the true cases of muscular deficiency in the group of boys and 75 per cent in the group of girls. This advantage is a direct result of the inclusion of arm girth in the formula.

Table 1 gave the comparative efficiency of different devices in the selection of true weight deviates. In table 2 the same devices are compared as to their selection of children with arm girth inappropriate to their skeletal type. In table 3 the devices are compared again, this time with the amount of subcutaneous tissue as the criterion. The A. C. H. screen is the best in this instance also. As shown in the three tables the A. C. H. screen is superior in all three manners of selection. Its superiority is large in the selection of "musculature deviates" and small but reliable in the other two respects. It is superior in the selection of children underweight, even though weight is not a part of the formula and is a part of the other two.

FINAL EVALUATION WITH AN INCLUSIVE CRITERION

The issue has been raised as to whether true deviation in weight should be used alone as a criterion. This issue may best be comprehended by viewing the coincidence of selections by weight, muscle and subcutaneous tissue. If all, or a large proportion of, the children showing a discrepancy in arm girth and subcutaneous tissue were also true weight deviates and vice versa, then it would not be necessary to use girth and caliper tests to include measurement of the soft tissue. But this is not the case. Of the 50 true "arm girth deviates" for boys only 19 had a deficiency in both weight and subcutaneous tissue,[6] 12 more had a deficiency in weight as well as in musculature, but the other 19 would never have been selected if weight alone were used as the measure. Twenty-two of the 55 with deficiency in the subcutaneous tissue would have been missed had weight alone been relied on.

It seems necessary to include all three qualities in the criterion. All three also should be made the goal for final selection. The severity of the line of demarcation may be decreased, and so may net more cases, but whatever the severity, a better all around selection is achieved by using all three. They are correlated, of course, but not so highly as to make it feasible to use any one alone. Comparison of the weight of children with that to be expected from their skeletal conformity—this alone, without consideration of muscle or subcutaneous tissue—is entirely inadequate as a basis for the selection of those who are malnourished.

6. Of course this does not entirely answer the question, since it depends on where the line of demarcation is drawn. However, if the line is drawn anywhere else it leads to the same conclusion.

If the objective is to find the children who show an overlapping deficiency in all three criteria—weight for skeletal build, arm girth for skeletal build and subcutaneous tissue for skeletal build—then judgment of the relative merit of the four selective methods must be based on their yield in these terms. The number of boys selected by this complete battery is 19, as was already mentioned. Of these 19, as shown in table 4, the weight-for-height method would yield 7; the height-hip-weight method, 12; the A. C. H. screen, 18, and the rating by a medical examiner, 5. Among the 24 girls, the A. C. H. screen would select 23. Thus, this screen reveals a distinct superiority to the other methods in the selection of children who show evidence of malnourishment when defined in the combined terms of weight, musculature and subcutaneous tissue.

TABLE 4.—*Comparison of Devices for Selection with True Deviation in Weight, Musculature and Subcutaneous Tissue as the Criterion*

Device	Number of Boys	Number of Girls	Total Numbers
Total criterion	19	24	43
Height-weight	7	9	16
Height-hip-weight	12	15	27
A. C. H. screen	18	23	41
Rating by medical examiner	5	*	*

* Medical ratings on the girls were not available.

The comparison in table 4 is made under conditions in which each of the original tests is set to pick about 1 of every 4 children for more intensive measurement. That is, in practice the A. C. H. screen is applied to an unselected group such as the 500 used in this experiment. The screen would pick about 125 from this number. Additional measures would then be applied to the 125 and the resulting selection would be the 41 cases shown in table 4. By this economical method all but 2 of the cases sought are detected. The time of measurement is about one third of the time that would be necessary to apply complete measurement and analysis to all 500 children.

SUMMARY

This paper points out the development of an abbreviated test suitable for practical application in schools. The illustration is limited to 11 year old children. A similar method is contemplated during the coming year for each of the other ages from 7 to 12 inclusive. The basic data necessary to do this are already at hand. Tables may then be issued for field use. Until such tables are available the adoption of this procedure in schools is not recommended.

CONCLUSIONS

1. Of four methods compared, the A. C. H. screen is the best extensive measure, whatever combination of weight, musculature and subcutaneous tissue is used as a criterion.

2. When the three criteria are used in combination, the A. C. H. screen is far superior to the other methods of selection. It then nets 41 of 43 (as yielded by the intensive survey) under conditions of selection which choose only 1 of 4 for intensive measurement. This compares to 27 and 16 netted by the other two objective methods.

3. Use of height-hip-weight devices are not adequate measures of weight or of malnutrition.

4. Comparisons of weight alone, even when skeletal build is taken into account, omit many marked deviations in the soft tissues.

IMMUNITY PRODUCED BY DIPHTHERIA TOXOID

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It is generally agreed that the most satisfactory method of active diphtheria immunization is the subcutaneous administration of diphtheria toxoid (diphtheria anatoxin-Ramon). The results of vaccination with this material have been very satisfactory. In 1929 the selection of all persons showing a positive reaction to the Schick test and their immunization by the use of diphtheria toxoid were established as a routine procedure in the St. Vincent's Infant Hospital. Vaccinations were done regardless of age as soon as a positive reaction was obtained, and the resultant immunity was measured by follow-up Schick tests at intervals of two weeks after the final injection. A preliminary report of the results obtained was published in 1931.[1] In 98 of this group of 100 infants, the reaction to the Schick test rapidly became negative and in 2 it remained persistently positive. Since then the total series has increased to 304; in 214 of these vaccination and subsequent Schick tests were carried out to completion. The longer period of observation has permitted the accumulation of data of additional interest in the evaluation of the method. These observations were carried out on a group of infants ranging in age from newly born to about 2 years. The infants were all immunized according to the original technic; i. e., two doses of 1 cc. each of commercial toxoid were administered subcutaneously at an interval of one week.

In 200 of the 214 infants studied, the reaction to the Schick test became negative and in 14 it remained persistently positive. Thus, 93.4 per cent of these infants responded to vaccination with the production of sufficient antitoxin to render their reaction to the Schick test negative. This percentage is somewhat less than that of the preliminary series, but still is very favorable and compares closely with the mass of statistics which is being accumulated.

DURATION OF IMMUNITY

French statistics concerning the persistence of artificial immunity produced by diphtheria toxoid are very favorable. Ramon and Debré [2]

From the University of Illinois School of Medicine, Department of Pediatrics.
Read as an inaugural thesis before the Chicago Pediatric Society, March 21, 1933.

1. Greengard, J.: Diphtheria Toxoid (Diphtheria Anatoxin Ramon) in Infancy, J. A. M. A. **97**:228 (July 25) 1931.

2. Ramon, G., and Debré, R.: Value and Duration of Immunity Conferred by Antidiphtheritic Anatoxin, Am. J. Dis. Child. **41**:1 (Jan.) 1931.

studied several groups of children who had been vaccinated more than one, two, three and four years previously, the groups being composed of 12, 26, 18 and 39 children, respectively. They found a high antitoxic content of the serum, over 0.1 unit per cubic centimeter, in 95 per cent of the three and four year groups, in 89 per cent of the two year group and in 82 per cent of the one year group. They stated that these figures show that the antitoxic content of the serum of vaccinated children does not diminish with time. The children in their series were all over 3 years of age. Thirty-seven of the earliest group received only two injections; all of the remainder received three. Lereboullet and Gournay [3] found a persistently negative reaction to the Schick test in 40 children vaccinated two years previously. Martin, Loisseau and Laffaille [4] vaccinated 91 children with a positive reaction to the Schick test with three doses of toxoid in 1926 and found them to give a negative reaction two years later. They also recorded a series of 400 children immunized from 1924 to 1928, 171 of whom were retested in March, 1929. All those whose reactions to the Schick test had become negative after two injections of toxoid (121) again revealed a negative reaction—in 6 after two years, in 1 after three years, in 18 after four years and in 97 after five years. In 1929 M. and G. Mozer [5] retested 910 vaccinated children at various intervals. They found positive reactions to the Schick test in 9 or 3.6 per cent of 250 vaccinated in 1925; in 7 or 4.3 per cent of 162 vaccinated in 1926, and in 25 or 5 per cent of 498 immunized in 1927. These figures correspond in a general way to the results obtained a few weeks after vaccination. The assumption was therefore drawn (by Ramon) that the immunity acquired persists for at least four years. In contrast to these findings are those of Frankl, Herzig and Nobel,[6] who found that the reaction to the Schick test reverted to positive in six months in 14 per cent of the children immunized by anatoxin. Accurate knowledge concerning this phase of the problem can be gained only after a considerable lapse of time, and as data are gathered they should be added to the literature.

In my group of 200 infants rendered immune during the past few years, 63 or 31.5 per cent remained in the institution long enough to be retested after vaccination. In 52 or 82.8 per cent of these 63 infants,

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3. Lereboullet, P., and Gournay, J.: L'immunisation anti-diphtérique par l'anatoxine à l'hôpital des enfants-malades, Ann. Inst. Pasteur **43**:181 (Feb.) 1929.

4. Martin, Soisseau and Laffaile, cited by Ramon, G.: L'anatoxine diphtérique dans son application à l'immunisation active de l'homme et à la prophylaxie de la diphtérie, Ann. Inst. Pasteur **45**:291 (March) 1930.

5. Mozer, M., and Mozer, G.: Quatre années de vaccination par l'anatoxine diphtérique à l'hôpital maritime de Berke, Presse méd. **37**:1543, 1929.

6. Frankl, G.; Herzig, H., and Nobel, E.: Ueber die Immunisierung gegen Diphtherie mit dem Ramon'schen Anatoxin, Wien. med. Wchnschr. **78**:1155, 1928.

the reaction remained persistently negative while in 11 or 17.2 per cent it became definitely positive. The duration of the immunity in these cases is given in table 1. In the 11 showing loss of immunity, 2 gave a definitely positive reaction to the Schick test less than six months after successful vaccination, while in 3 children, immunity lasted a year or more and then sank below the Schick level. In the 52 showing persisting immunity, 23 continued to show negative reactions a year or more after vaccination and 1 as long as twenty-nine months later. All these children were in the same environment during the entire period of observation. During this time there was practically no clinical diphtheria in the institution. Dudley [7] suggested that the absence of more or less frequent antigenic stimuli from diphtheria bacilli in the environment may result in a drop in antitoxic titer of the serum below the Schick level. In this respect he expressed the need for more observations from rural districts on the stability of immunity as demonstrated by the Schick test. This factor may be of importance in the rapid loss of immunity in the 11 infants of this series.

TABLE 1.—*Duration of Immunity (63 Cases)*

	Months After First Negative Reaction Following Vaccination																	
	4	5	6	7	8	9	10	11	12	13	14	15	16	18	20	22	23	29
Persistent negative reaction...	..	..	9	5	7	3	3	3	5	6	1	1	1	1	2	4	1	1
Recurring positive reaction....	1	1	..	3	..	..	1	2	1	..	..	2	..	..	..	..	..	..

AGE AND THE PERSISTENCE OF IMMUNITY

This experiment deals with a group of very young children. It has been shown that young animals form antibodies poorly. Park [8] stated that attempts to produce diphtheria immunity with toxin-antitoxins are not advisable before 6 months of age. He ascribed the failure of production of antitoxin to the fact that younger children still retained their passive immunity, and thus overneutralization of the toxin-antitoxin occurred. Ribadeau-Dumas, Loisseau and LaComme [9] vaccinated 15 infants with diphtheria anatoxin. Thirteen of these were under 9 months of age; 1 was 22 months old, and 1 child 2 years old. Only 3 responded with an increase in the antitoxin titer of the serum. Freund [10] investigated the production of agglutinins against typhoid bacilli, hemo-

7. Dudley, S. F.: The Schick Test and Its Application, Quart. J. Med. **22**: 321, 1929.

8. Park, cited by Blum.[12]

9. Ribadeau-Dumas, L., Loisseau, and LaComme: La vaccination antidiphtérique des nourrissons, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1121, 1925.

10. Freund, J.: Influence of Age upon Antibody Formation, J. Immunol. **18**: 315, 1930.

lysins against sheep corpuscles and precipitins against horse serum and egg white in rabbits less than 20 days old. He found that such young animals formed immune bodies much less intensely than adult animals immunized in the same way. Nattan-Larrier and Ramon [11] inoculated new-born rabbits and their mothers with tetanus anatoxin. The new-born animals formed antitoxin, but to a much less degree than their mothers. These authors stated that this is due to the inability of the new-born animal to form antibodies well. In a recent report Blum [12] stated that from one fourth to one third of infants under 9 months of age fail to respond to immunization with toxin-antitoxin mixtures. He inoculated the infants irrespective of age and without preliminary Schick tests. While his data are of great practical value, since they demonstrate the fallacy of routine vaccination without preliminary testing in young age groups, they do not demonstrate accurately the ability

TABLE 2.—*Relationship of Age to Production of Immunity (214 Cases)*

	Age at Which Vaccination Was Done					
	Under 1 Month	1 to 3 Months	3 to 6 Months	6 to 9 Months	9 to 12 Months	Over 1 Year
Reaction rendered negative....	20 (10%)	31 (15.5%)	62 (31%)	50 (25%)	16 (8%)	21 (10.5%)
		56.5%			43.5%	
Persistent positive reaction....	3 (21.4%)	2 (14.2%)	8 (57.1%)	0	0	1 (7.2%)
		92.8%			7.2%	

of the infants of the various age groups to form antibodies. In a small group of infants, Park and Shroder [13] were able to immunize between 90 and 100 per cent of those over 3 months of age, while the younger age groups showed poorer results. Here also a preliminary Schick test was omitted. They concluded that the infant may be immunized after 3 months of age.

In view of these data, the relationship of the age of the subject to the production and duration of immunity in this series is of interest. Table 2 shows the group of 14 infants who failed to develop sufficient antitoxic immunity following vaccination to raise them above the Schick level. It will be noted that with one exception all of these infants were

11. Nattan-Larrier, L.; Ramon, G., and Grasset, E.: L'anatoxine tétanique et l'mmunité antitétanique chez la mère et le nouveau-né, Ann. Inst. Pasteur **41**:848, 1927.

12. Blum, J.: Age Factor in the Active Immunization of Infants Against Diphtheria, J. A. M. A. **98**:1627 (May 7) 1932.

13. Park, W. H., and Shroder, M. C.: Diphtheria Toxin Antitoxin and Toxoid, a Comparison, Am. J. Pub. Health **22**:7, 1932.

under 6 months of age. The age distribution of the 200 children successfully vaccinated showed a more even distribution, 56.5 per cent being under 6 months and 43.5 per cent over 6 months of age.

The 63 infants retested after vaccination are grouped as shown in table 3. Of the 11 whose reaction became positive, 9 were under 3

TABLE 3.—*Schick Reaction Following Vaccination*

Age	Number of Children	Remained Negative	Reverted to Positive
Under 3 months	17	8 (47.1%)	9 (52.9%)
3 to 6 months	22	21 (95.5%)	1 (4.5%)
6 to 12 months	20	20 (100%)	0 (0%)
Over 1 year	4	3 (75%)	1 (25%)

months of age; of the 46 infants over 3 months of age 44 retained their immunity. This confirms the laboratory data reported in the literature and indicates that infants under 3 months of age apparently do not form antibodies well. Even with a potent immunizing agent such as diphtheria toxoid, which is capable of rendering a positive Schick reaction negative in these young infants, the immunity so produced is of short duration. The advisability of attempting immunization in very young infants may therefore be questioned. In institutions, however, such a practice is justified, as it is desirable for the entire population to maintain a negative Schick reaction. As a general practice, however, it is probably well to withhold immunization until after 6 months of age.

RAPIDITY OF PRODUCTION OF IMMUNITY AND ITS DURATION

In reviewing the 63 cases in which follow-up Schick tests were possible one finds data which suggest that the more rapidly the immunity is produced the more likely it is to be lasting. In other words, those

TABLE 4.—*Relationship of the Rapidity of the Production of Immunity to Its Persistence*

	Interval Between Second Injection of Toxoid and First Negative Schick Reaction						
	2 Weeks	4 Weeks	6 Weeks	8 Weeks	10 Weeks	12 Weeks	16 Weeks
Reverting to positive reaction (11 cases)	1 (9%)	4 (36.3%)	4 (36.3%)	1 (9%)	1 (9%)		
Persistent negative reaction (52 cases)	27 (51.9%)	10 (19.2%)	6 (11.5%)	1 (1.9%)	3 (5.7%)	2 (3.8%)	2 (3.8%)

persons in whom antitoxin is formed well respond to their antigenic stimuli with a rapid production of large amounts of antitoxin. In the 52 cases in which the reaction remained persistently negative, 27 or 51.9 per cent showed a negative Schick reaction two weeks after the

second dose of diphtheria toxoid. On the contrary, of the 11 cases in which the reaction became positive, only 1 (9 per cent) showed a negative reaction after so short an interval (table 4). This finding, if confirmed in a large series of cases, may be of significance.

TYPE OF TOXOID USED AND IMMUNITY PRODUCED

The principal advantage of toxoid over toxin-antitoxins in active immunization against diphtheria lies in the fact that a nontoxic and stable substance of higher antigenic potency is made available. However, there may be considerable variation in potency in various samples of toxoid. The efficiency of such preparations may be tested by animal experimentation or by the simple and accurate flocculation reaction devised by Ramon.[14]

The results of immunization of children vary definitely with the antigenic potency of the toxoid used. Thus Ramon and Nelis[15] obtained superior results with toxoids of high antigenic potency as compared with toxoids of lower potency. They vaccinated a group of 269 children with anatoxins of 7 and 4.5 units and obtained 80 per cent immunity. In 293 parallel cases using anatoxins of 16 and 12.5 units, 94.2 per cent were rapidly rendered immune.

In this series I have been able to observe a similar result, which has been reported in detail elsewhere.[16] In brief, two series of infants were vaccinated with toxoids which later proved to be of low antigenic potency. The Schick reaction became negative in 85.8 per cent of the first series, and in only 80 per cent of the second series. In comparison with the general average of 93.4 per cent the disadvantage of the weaker mixture is apparent. Povitzky[17] examined several products of different manufacturers, using the flocculation reaction as a test of antigenic potency. He found great variability in the samples tested. One toxoid yielded from 6.8 to 7 antigenic units per cubic centimeter, one 4.4 units and one 4.2 units. Two diluted samples showed no antigenic units, and one undiluted toxoid showed no flocculation, though kept in the water bath almost a week. This laboratory finding is in complete accord with my clinical results. It is therefore essential that the material used in active immunization be of known high antigenic potency.

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14. Ramon, G.: The Essential Properties of Diphtheria Anatoxin, French M. Rev. **2**:13 (Jan.) 1932.

15. Ramon, G., and Nelis, P.: Essais d'immunisation active chez l'homme au moyen d'une anatoxine diphtérique de valeur antigène elevée, Compt. rend. Soc. de biol. **107**:487, 1931.

16. Greengard, J.: The Effectiveness of Commercial Diphtheria Toxoid in the Immunization of Infants, J. A. M. A. **100**:793 (March 18) 1933.

17. Povitzky, O. R.: Degree of Immunization from Injection of Diphtheria Toxoid, Am. J. Pub. Health **22**:29, 1932.

COMMENT

There are several special features of the immunizing procedure recorded here. In this group of children toxoid was given in but two doses, with a short interval between the injections. Ramon and his co-workers found that in general better results were obtained when a longer interval was allowed between doses, and when the dosage was increased to three injections. Their recommended dosage at the present time consists in three injections of 0.5, 1 and 1.5 cc. of diphtheria toxoid with an interval of three weeks between the first and second injections and two weeks between the second and third. Povitzky found in his animal experiments that the same dose of toxoid given in two or three parts at weekly intervals conferred a higher degree of immunity than when given in a single dose. The degree of immunity was still further enhanced when the second dose was given three weeks after the first and the third dose two weeks after the second. It was impossible to carry out immunization to completion with such a long interval in the majority of my cases since many of the children left the wards before the subsequent vaccinating doses and follow-up Schick tests could be given. Since it was deemed desirable to immunize the infants as rapidly as possible and to know with a degree of certainty just which children were susceptible and which immune at all times, the technic of two injections with a sort interval was adopted. It is of interest that under these circumstances the number in which the Schick reaction became negative was high.

In this connection the potency of the product used is of great importance, a fact which is not sufficiently appreciated. This has been conclusively shown by Ramon and Nelis and in this series. Povitzky found that with different toxoids the degree of immunity produced increased with the number of antigenic units per cubic centimeter of toxoid used. In France the potency of the anatoxins used is at least 10 antigenic units per cubic centimeter. The toxoid used by the New York Health Department also averages about 10 units. In America, the commercial material distributed is apparently of much more variable potency. When the strength of the material used is not indicated on the package, it is dangerous to consider vaccination complete without routine follow-up Schick tests.

The second special feature of this group lies in the fact that immunization was carried out in very young infants. This fact must be taken into consideration in evaluating the results. As I mentioned before, it has been shown that very young animals form antibodies badly. In my group the infants who failed to respond to vaccination with sufficient antitoxin to render their reaction to the Schick test negative, with 1 exception, fell in the age group under 6 months. In

addition, of those immunized infants who reverted to a positive reaction later, all but 1 were immunized under 6 months of age. In other words, when these young infants do respond to the antigenic stimuli with sufficient antitoxin to raise them above the Schick level, the immunity produced is of relatively short duration in a high percentage of cases. If infants under 6 months of age are excluded from the series, the results are quite different, yielding a much higher percentage of those rendered immune and demonstrating the persistence of immunity in all but 1 case. This is in close agreement with the French literature on persistence of immunity. In other words, the loss of immunity in the 11 cases observed is not to be attributed to lack of antigenic potency of the agent used, but to an inherent peculiarity of the subject, dependent on age.

The rapidity of production of immunity is also linked with age. It was found that of the 11 infants who reverted to a positive reaction only 1 showed a negative reaction to the Schick test in two weeks. In other words these very young infants form antibodies more slowly than older children and quantitatively less. The lack of repeated antigenic stimuli in the environment may also be a contributing factor in the loss of immunity, as has already been noted. These infants have all received a primary antigenic stimulus and, as shown by Glenny,[18] should respond to any subsequent stimulus with a rapid and profuse production of antitoxin. Three of the 11 children whose reactions reverted to positive were given a single 1 cc. dose of toxoid, and all 3 then demonstrated a negative reaction to the Schick test, nine months, eight months and eight months after the third injection.

CONCLUSIONS

1. In a series of 214 susceptible infants ranging from newly born to 2 years of age, 93.4 per cent showed a negative reaction to the Schick test after two injections of 1 cc. of commercial diphtheria toxoid.

2. Of 63 immunized infants retested at intervals after the first negative reaction to the Schick test, 11 or 17.2 per cent reverted to a positive reaction.

3. Of the 14 infants who failed to demonstrate a negative reaction to the Schick test after vaccination, 13 were immunized during the first half year of life. Of the 11 immunized infants whose reactions reverted to positive, 10 were immunized when under 6 months of age.

4. In the small group of infants in whom the duration of immunity could be tested, it was noted that the immunity seemed more lasting in the infants who demonstrated immunity to the Schick test most rapidly.

18. Glenny, A. T.: The Principle of Immunity Applied to Protective Inoculation Against Diphtheria, J. Hyg. **24**:301, 1925.

5. There is a definite relationship between the antigenic power of the immunizing agent used and the results of vaccination.

6. Immunization should never be considered complete without a follow-up Schick test.

185 North Wabash Avenue.

DISCUSSION

DR. M. L. BLATT: The importance of this careful evaluation of toxoid has been demonstrated by the absence of clinical diphtheria at St. Vincent's Orphange since Dr. Greengard undertook the work. This is significant in view of the fact that this orphanage is crowded with persons susceptible to the disease. There is a constant change of personnel among these dependent children, and they are frequently exposed to new attendants and nurses. Prior to Dr. Greengard's interest in the problem, small epidemics of diphtheria occurred frequently.

DR. JOSEPH GREENGARD: The toxoid furnished by the state of Illinois for my work has been satisfactory.

Case Reports

DISTURBANCE IN GLYCOGEN METABOLISM WITH HEPATOMEGALY

(VON GIERKE'S DISEASE)

LOUISE RAUH, M.D.
AND
CARL ZELSON, M.D.
NEW YORK

In 1929, von Gierke [1] first described a syndrome which he called glycogenic hepatonephromegaly. He reported the cases of two patients, aged 8 and 4½ years, both of which came to autopsy undiagnosed. The postmortem examination revealed, in both cases, a tremendously enlarged liver, moderately enlarged kidneys and, in one case, hypoplastic suprarenal glands. Microscopically, the cells of the liver and of the collecting tubules of the kidneys were packed with glycogen.

Since this report was published, four cases of a similar nature have been described. At present we have under observation, at the Mount Sinai Hospital, a child whose history, physical examination, clinical course and laboratory data in many ways resemble those of the cases previously reported. We feel that the case is of sufficient interest to be reported and compared with the seven other cases found in the literature.

REPORT OF CASE

History.—The patient, an Italian boy, aged 20 months, was admitted to the pediatric service of the Mount Sinai Hospital on July 14, 1932, with a history that at the age of 8 months his abdomen seemed to be larger than normal, and that for the past twelve months it had been increasing in size. There had been no other complaints. The family history and the patient's birth and history prior to admission were unimportant. There had been no history of syphilis. The patient's development had been normal.

Physical Examination.—The patient, a rather pale child, was fairly well nourished but somewhat stunted in growth. He was 74 cm. (29.6 inches) in length and weighed 9,180 Gm. (20 pounds and 2 ounces); the sitting height was 50 cm. (20 inches). The child seemed bright, active and comfortable. The

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From the service of Dr. B. Schick, Mount Sinai Hospital.

1. von Gierke, E.: Hepato-Nephromegalia glykogenica (Glykogenspeicherkrankheit der Leber und Nieren), Beitr. z. path. Anat. u. z. allg. Path. **82**:497, 1929.

skeletal system was normal. Some of the cervical, inguinal and axillary glands were slightly enlarged. The heart and lungs were normal. The abdomen was markedly large and protuberant, measuring 52 cm. (20.8 inches) in circumference. The edge of the liver was felt at about 5 cm. below the umbilicus in the right mammillary line, slanting upward toward the left, crossing the midline at the level of the umbilicus and extending to about 5 cm. to the left of the midline, where a notch was felt. This notch seemed to divide the left from the right lobe; the left lobe extending about 7 cm. below the costal margin in the left mammillary line. The liver was somewhat movable and firm and was not tender. The edge was sharp and the surface smooth. The spleen was not felt, nor were any masses palpable under the liver. The physical examination of the child was otherwise unimportant.

Fig. 1.—The patient at the age of 26 months (January, 1933). The edge of the liver is outlined.

Laboratory Data.—The urine showed acetone on repeated examinations. On two occasions, by comparison with two normal children, the diastatic ferment was found to be in great excess. In a twenty-four hour specimen on another occasion, 19 units of amylase was found (method of Elman).[2] No free glycogen was found in the urine on two determinations (polariscope). There was no glycosuria following the ingestion of 40 Gm. of dextrose. The blood amylase was 0.9 units (Elman method; from 2 to 6 units normal). No free glycogen was found in the blood on two examinations. The blood sugar during fasting varied between 40 and 65 mg. per hundred cubic centimeters. Two tests for sugar tolerance were made

2. Elman, R.; Arneson, N., and Graham, E. A.: Value of Blood Amylase Estimations in Diagnosis of Pancreatic Disease, Arch. Surg. **19**:943 (Dec. pt. 1) 1929.

(fig. 2). In the first test, 20 Gm. of dextrose (1 Gm. per kilogram) was given. The blood sugar during fasting was 50 mg.; half an hour after the ingestion of dextrose it was 90 mg.; one hour after, 80 mg.; one and a half hours after, 95 mg.; two hours after, 110 mg., and three hours after, 70 mg. In the second test, 36 Gm. of dextrose (2 Gm. per kilogram) was given. The blood sugar during

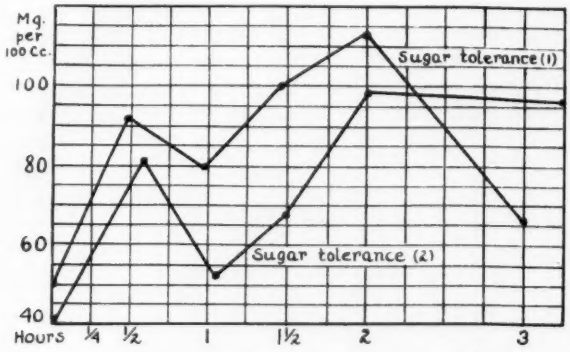

Fig. 2.—Results of two tests for sugar tolerance.

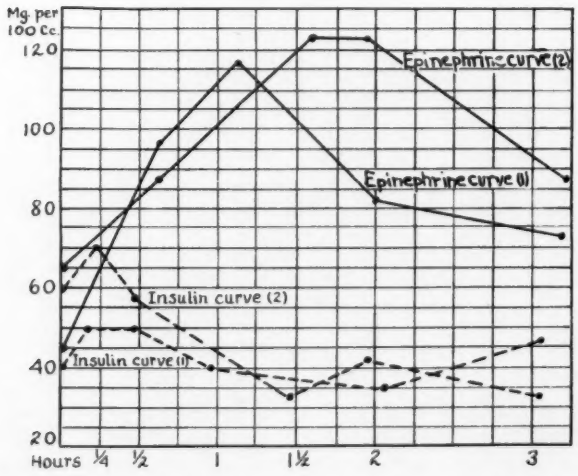

Fig. 3.—Response of the blood sugar to epinephrine on two occasions.

fasting was 40 mg.; half an hour after the ingestion of dextrose, it was 80 mg.; one hour after, 50 mg.; one and a half hours after, 70 mg.; two hours after, 100 mg., and three hours after, 100 mg.

On two occasions the blood sugar response to epinephrine was determined (fig. 3). In the first test, 0.3 cc. of a 1:1,000 solution of epinephrine was given subcutaneously, and specimens of blood were examined over a period of three hours. The initial blood sugar was 45 mg. per hundred cubic centimeters; half an hour after the epinephrine was given, it was 95 mg.; one hour later, 115 mg.; two hours later, 80 mg.; three hours later, 75 mg. In the second test, we used 0.5 cc. of

epinephrine. The initial blood sugar was 65 mg.; half an hour after the injection, it was 85 mg.; one hour after, 105 mg.; one and a half hours after, 120 mg.; two hours after, 120 mg., and three hours after, 95 mg.

The blood sugar response to insulin was determined on two occasions (fig. 2). In the first test, 2 units of insulin was injected subcutaneously. The blood sugar during fasting was 40 mg.; fifteen minutes after the injection of insulin, it was 50 mg.; thirty minutes after, 50 mg.; one hour after, 40 mg.; two hours after, 35 mg,. and three hours after, 50 mg. In the second test we used 5 units of insulin. The initial blood sugar was 60 mg.; fifteen minutes after the injection of insulin, it was 70 mg.; half an hour after, 55 mg.; one hour after, 45 mg.; one and a half hours after, 35 mg.; two hours after, 45 mg., and three hours after, 35 mg.

The blood urea nitrogen was 17 mg. per hundred cubic centimeters; total cholesterol taken on three occasions was 310, 415 and 395 mg., with the cholesterol ester 185 mg., 120 mg. and 290 mg., respectively. The blood calcium was 10.8, and the phosphorus, 4.8 mg. per hundred cubic centimeters. The icteric index was 6, and the van den Bergh tests, direct and indirect, were negative. After 25 Gm. of galactose had been given by mouth, only a faint trace was excreted in the urine collected over a period of five hours. The bromsulphophthalein test showed no impairment in hepatic function.

Examination of the blood showed hemoglobin, 70 per cent; red cells, 3,900,000, and white cells, 16,600, with 32 per cent polymorphonuclears, 58 per cent lymphocytes, 6 per cent monocytes and 4 per cent eosinophils. A Best stain of the blood smear showed no glycogen deposit in the leukocytes. A Wassermann test of the blood was negative on two occasions. The stools were normal. The Pirquet and Mantoux tests up to 1 mg. were negative. The echinococcus skin test and roentgenograms of the chest gave negative results. Roentgenograms of the long bones showed transverse lines in the metaphysis indicating former retardation in growth.

Clinical Course.—Shortly after admission, the patient was given a diet high in carbohydrates for a period of twenty-three days, but no increase in blood sugar or change in the size of the liver was evidenced. He was then given a well balanced mixed diet, on which he was kept for the remainder of his stay in the hospital.

Because the suprarenal glands in one of von Gierke's cases were found to be hypoplastic at autopsy, we began a course of treatment with epinephrine. We gave 0.2 cc. of a 1:1,000 solution of epinephrine subcutaneously twice daily over a period of eight days. Neither a prolonged elevation in the blood sugar nor a decrease in the size of the liver was effected.

The child was observed for one week after the discontinuance of the injections of epinephrine; there was no apparent change. Treatment with thyroid was instituted, in the hope of liberating glycogen from the liver and thus raising the level of the blood sugar. We began with 0.006 Gm. of desiccated thyroid by mouth three times daily. Increments were made every four days, so that after eighteen days the dosage was 0.12 Gm. three times daily. This dosage was continued for nine days. Except for the fact that the child lost 500 Gm. (1.1 pounds) in weight, there was no marked change; the size of the liver remained the same, and the blood sugar during fasting remained around 40 mg.

The child was in the hospital for three months, during which time he grew 3 cm. in height and gained 1,800 Gm. (4 pounds). The circumference of his abdomen increased 4 cm. (1.6 inches). A mild eczema developed on the face, which persisted. At no time was there any spontaneous hypoglycemic reactions, but the

breath frequently had an odor of acetone. It is of interest to note that the child preferred foods high in carbohydrates, particularly potatoes. At the time of discharge, his condition was the same as on admission.

After three weeks at home he was readmitted for a mild infection of the upper respiratory tract. There was no change in the clinical picture.

DISCUSSION OF CASE

The striking features of this case are the hepatomegaly, the acetonuria, the low blood sugar during fasting, the abnormal curve for sugar tolerance, the low blood diastase and the high urinary diastase. The curves for sugar tolerance were definitely abnormal in that both were diphasic in character and remained elevated over a prolonged period of time. The response to epinephrine and insulin, as evidenced by the blood sugar curves, was normal.

There was no evidence of disturbance in the function of the liver judged on the basis of the galactose and bromsulphophthalein tests. In addition, the ratio of the cholesterol ester to the total cholesterol was normal in two of three determinations. We are unable to explain the significance of the increased total cholesterol. We shall discuss the low blood and the high urinary amylase later.

In arriving at our diagnosis of hepatomegaly due to a disturbance in the glycogen metabolism, we considered and eliminated other conditions as follows:

Echinococcus cyst, hemangioma and congenital cystic liver are not accompanied by hypoglycemia and acetonuria. In addition, the echinococcus skin test was negative. Hemangioma of the liver was further ruled out by the absence of telangiectasia elsewhere and by the general conformation of the liver, together with the fact that hemangiomas usually begin to enlarge at puberty.

The two negative Wassermann examinations of the blood and the absence of other syphilitic stigmas made the diagnosis of syphilis improbable.

We felt that hepatic infantilism is not a definite clinical entity and agree with Goettche [3] that infantilism may accompany any type of chronic hepatic disease as it does chronic intestinal, cardiac or renal diseases. Von Pfaundler [4] found underdevelopment in all cases of cirrhosis of the liver in childhood.

Hyperinsulinemia was first described by Wilder [5] in a case of carcinoma of the islands of Langerhans. All cases of this sort that have been described have occurred in adults and are associated with a severe spontaneous hypoglycemia becoming progressively worse. At no time was a hypoglycemic reaction observed in our case.

Spontaneous hypoglycemia was first observed by Harris [6] in adults. Elias and Turner [7] noted the same condition in four children. All of these showed severe spontaneous hypoglycemic reactions with unimportant findings in physical examinations.

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3. Goettche, O.: Ein Fall von "hepatischem Infantilismus," Monatschr. f. Kinderh. **35**:505, 1927.

4. von Pfaundler, M.: Hepatischer Infantilismus (?) Ztschr. f. Kinderh. **41**: 78, 1926.

5. Wilder, R. M.; Allan, F. N.; Power, M. D., and Robertson, H. E.: Carcinoma of the Islands of the Pancreas, J. A. M. A. **89**:348 (July 30) 1927.

6. Harris, S.: Hyperinsulinism and Dysinsulinism, J. A. M. A. **89**:729 (Sept. 6) 1924.

7. Elias, H. L., and Turner, R.: Spontaneous Hypoglycemic Shock in Children, J. A. M. A. **98**:2198 (June 18) 1932.

A diagnosis of cirrhosis of the liver was not definitely ruled out, but the absence of jaundice, ascites and enlargement of the spleen, the normal icteric index and the negative reaction to the van den Bergh tests, together with the absence of urobilin in the urine and the tests showing normal hepatic function, all of which were associated with our positive findings, spoke against such a diagnosis.

REVIEW OF CASES REPORTED IN THE LITERATURE

We shall give only a brief clinical summary of the cases reported. The laboratory data for each case can be found in the accompanying table.

The well known case of Wagner and Parnas [8] reported in 1921, eight years before von Gierke's publication, must be included in this series because it presents so many features in common with the other cases described. At the time of that report, Wagner and Parnas felt that they were dealing with a metabolic disturbance in which the liver was unable to store glycogen, and in which the thyroid was hypo-active. Since then, Priesel and Wagner, in their book, "Diabetes in Childhood," [9] have expressed the belief that this case belongs to the group which we are describing.

The patient, a 9 year old girl, was admitted with the history that at the age of 3 months enlargement of the liver had been noted. At 4 years, antisyphilitic treatment had been given, in spite of a negative reaction to the Wassermann test, but without improvement. On examination, the child was found to be markedly underdeveloped, and the abdomen much enlarged, being almost completely filled by the liver. The rest of the examination disclosed nothing of importance. At the age of 16 years, true diabetes mellitus developed.

Three years after von Gierke described his cases, in February, 1932, van Creveld [10] reported a case of what he termed chronic hepatogenous hypoglycemia in childhood. The patient was a boy, aged 10 years, with a history of a large abdomen progressively increasing in size since birth. At the age of 1½ years, an exploratory laparotomy was done, and a large, smooth liver was found. No biopsy was performed. The child was underdeveloped and gave the impression of having adiposogenital dystrophy. Except for a very large liver, the results of physical examination were negative.

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8. Wagner, R., and Parnas, J. K.: Ueber eine eigenartige Störung des Kohlenhydratstoffwechsels und ihre Beziehung zum Diabetes mellitus, Ztschr. f. d. ges. exper. Med. **25**:361, 1921.

9. Priesel, R., and Wagner, R.: Die Zuckerkrankheit und ihre Behandlung im Kindesalter, Leipzig, Georg Thieme, 1932.

10. van Creveld, S.: Chemische hepatogene Hypoglykämie im Kindesalter, Ztschr. f. Kinderh. **52**:299, 1932.

A few months later, in May of the same year, Bischoff [11] reported the case of a girl, aged 4 months, in whom postmortem examination revealed a very large heart, a moderately enlarged liver and hypoplastic suprarenal glands. The microscopic examination of the heart revealed

Brief Clinical Summary

Authors	Sex	Age	Enlargement of the Liver First Noted	Physical Examination	Development	Urine	Blood Sugar During Fasting, Mg. per 100 Cc.	Glycogen, of the Blood, Mg. per 100 Cc.	Diastase of the Blood
Wagner and Parnas 1921	♂	9 yrs.	3 mos.	Large liver	Retarded	Acetone; diacetic acid; glycosuria	0+	.....	.....
von Gierke I 1929	♀	8 yrs.	2-3 mos.	Large liver	Normal	Negative	....	30-40 in 15 cc., 6 days post mortem	.....
von Gierke II 1929	♂	4½ yrs.	?	Large liver	?	?	....	.....	.....
van Creveld 1932	♂	10 yrs.	Birth	Large liver; adiposo-genital dystrophy	Retarded	Acetone; beta-oxybutyric acid	30-64	13.7-25.1	.....
Bischoff 1932	♀	4 mos.	Birth	Very large heart; moderately enlarged liver	Normal	Negative	....	.....	.....
Loeschke 1932	♂	3 yrs.	8 mos.	Large liver	Slightly retarded	Acetone; excess diastase	52-95	17.4	Low
Unshelm 1932	♂	19 mos.	3-4 wks.	Large liver; rickets	Retarded	Acetone; diacetic acid; excess diastase; glycosuria	70	0	Increased 17 hours post mortem
Rauh and Zelson 1933	♂	20 mos.	8 mos.	Large liver	Retarded	Acetone; excess diastase	40-65	0	Low

huge deposits of glycogen in the muscle fibers. The liver contained some glycogen, even though the tissue had been in formaldehyde for three weeks (Putschar).[12]

11. Bischoff, G.: Zum klinischen Bild der Glykogen-Speicherungskrankheit (Glykogenese), Ztschr. f. Kinderh. **52**:722, 1932.

12. Putschar, W.: Ueber angeborene Glykogen-Speicherungskrankheit des Herzens-"Thesaurismosis glycogenica" (von Gierke), Beitr. z. path. Anat. u. z. allg. Path. **90**:322, 1932.

In September, 1932, Loeschke [13] reported a case in which for the first time the diagnosis was confirmed by biopsy. The patient was a boy, aged 3 years, who came under observation because of an enlargement of the liver which had first been noted at the age of 8 months. Because

of Cases Reported

Blood Cholesterol, per 100 Cc.	Tests of Hepatic Function	Sugar Tolerance Test	Response of Blood Sugar to Epinephrine	Response of Blood Sugar to Insulin	Spontaneous Hypoglycemic Reactions	Course	Biopsy	Autopsy
.....	.....	Diabetic curve	Slight	.....	Absent	Diabetes mellitus at 16 yrs.		
.....	.....	.....	.....	.....	.....	Death due to grip	.....	Large liver; large kidneys; hypoplastic suprarenal glands; cells of liver and kidneys filled with glycogen
.....	.....	.....	.....	.....	.....	Death due to pneumonia	.....	Same except for normal suprarenal glands; cells of liver and kidneys filled with glycogen
227 mg. in the total blood; 435 mg. in the plasma	Sugars normal	Prolonged elevation; biphasic	Slight	Sudden drop in blood sugar with shock due to insulin	Absent	Living, somewhat improved		
.....	.....	.....	.....	.....	.....	Death due to pneumonia and cardiac decompensation	.....	Large heart; moderately large liver; hypoplastic suprarenal glands; cells of heart and liver filled with glycogen
.....	Galactose test normal	Similar to that in diabetes; biphasic	Slight	Steep drop in blood sugar; shock due to insulin	Present	Living	Showed liver cells filled with glycogen	
.....	.....	.....	.....	.....	Absent	Death due to pneumonia	.....	Large liver; cells of liver, heart, striated muscle and brain filled with glycogen; few islets of Langerhans showing degeneration
310-420 mg.; ester, 120-285 mg.	Galactose and bromsulphphalein tests normal	Prolonged elevation; biphasic	Good	Moderate drop in blood sugar	Absent	Living		

of a family history of syphilis, the child had received antisyphilitic treatment, but without improvement. Aside from a slight retardation in growth and enlargement of the liver, the physical examination revealed no abnormality.

The biopsy of the liver showed cells markedly swollen and enlarged. With Best's stain, the enlargement was found to be due to enormous droplets of glycogen which almost filled the cell (Putschar [12]).

13. Loeschke, A.: Zur Klinik der Glykogen-Speicherungskrankheit (von Gierkeschekrankheit), Ztschr. f. Kinderh. **53**:553, 1932.

Recently, in December, 1932, Unshelm [14] reported a case in a boy, aged 19 months, who came under observation at the age of 7 months because of progressive enlargement of the abdomen since the age of 3 weeks. The child was markedly underweight, underdeveloped and mentally retarded. Aside from a tremendously enlarged liver, rickets and a mild eczema, the results of the physical examination were unimportant. The child died of pneumonia, and postmortem examination revealed a huge liver, with an excessive amount of glycogen within the cells of the liver, heart, striated muscles and brain. A few of the islands of the pancreas appeared abnormal.

The family history in this case is of importance. One brother, who presented a similar clinical picture, died at the age of 20 months. No cause for the enlargement of the liver was found, in spite of an exploratory laparotomy. Though the lack of laboratory data and the absence of a postmortem examination make it difficult to include this case in our series, the history and findings in the other child point out the possibility of this disease being one of familial nature.

COMMENT

The two cases of von Gierke and the case of Bischoff came to autopsy without having aroused a suspicion of the underlying pathologic process. Only five of the eight cases described, therefore, have been thoroughly studied. These presented a number of characteristics in common: a large liver noted in the first year of life, hypoglycemia, acetonuria, physical underdevelopment and a mentality corresponding to age, except in two cases in which it was low.

In analyzing the cases further, we find that in no case was the curve for sugar tolerance normal; thus a faulty carbohydrate metabolism was indicated. Four cases showed a prolonged elevation of blood sugar; three, a biphasic reaction, and two, a diabetic curve. No sugar tolerance test was performed by Unshelm. The response of the blood sugar to epinephrine was slight in three cases and normal in our case. The absence of a response to epinephrine in the presence of a normally functioning thyroid gland indicates the presence of immobilizable glycogen in the liver. In only Wagner and Parnas' case was there a question of disfunction of the thyroid gland, and this they based on very low blood sugar during fasting and a refractory response to medication with thyroid extract.

The fact that we obtained a good response to epinephrine is difficult to explain unless we consider that the disease is in an early stage and that a fair amount of glycogen can still be liberated, or that there is a great deposit of glycogen in the muscles which can be utilized. Cori

14. Unshelm, E.: Die Glykogenkrankheit (Zugleich ein Beitrag zur Frage des hepatogenen Infantilismus), Jahrb. f. Kinderh. **137**:18, 1932.

and Cori [15] showed that in rats the injection of epinephrine decreased the glycogen in the muscles, at the same time increasing the content of glycogen in the liver. Jacobson,[16] in his studies on carbohydrate tolerance, concluded that muscles can undoubtedly perform the function of glycogenesis and glycogenolysis.

We obtained only a moderate reduction in the blood sugar following insulin, whereas van Creveld and Loeschke found a sudden drop in blood sugar accompanied by shock.

The cholesterol in the blood was increased in both of the cases in which it was determined. The glycogen in the blood was increased in two cases but absent in ours. In von Gierke's case, Schönheimer [17] found an increase in the glycogen of the blood six days post mortem. The amylase in the blood obtained in two cases was low as compared with that of normal children. Unshelm found an increase of amylase in the blood of a person examined seventeen hours post mortem.

The tests with sugars for function of the liver gave negative results in three cases. In addition, the bromsulphophthalein test in our case was normal.

Glycosuria was absent in all the patients except two, and in one of these a true diabetes mellitus subsequently developed. Urinary amylase was increased in the three cases in which it was estimated.

The Wassermann test of the blood was negative in all cases. Two of the patients received antisyphilitic treatment, with no improvement.

Four cases came to postmortem examination. A large liver was found in all four, hypoplastic suprarenal glands in two, enlarged kidneys in two and tremendously enlarged heart in one. On microscopic examination, the cells of the various enlarged organs were found to be loaded with glycogen. The biopsy of the liver in Loeschke's case showed cells presenting a similar microscopic picture. In addition, Unshelm found an increase in the glycogen content of the cells of the brain and striated muscle.

Three cases which we have not included in our series, but which we feel should be mentioned because of their similarity, were reported by Exchaquet in 1931,[18] under the title of "Familial Hepatic Infantilism."

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15. Cori, C. F., and Cori, G. T.: Influence of Epinephrine on Carbohydrate Metabolism, Proc. Soc. Exper. Biol. & Med. **25**:258, 1928.

16. Jacobson, C.: Carbohydrate Tolerance in Eck Fistula, Am. J. Physiol. **52**:233, 1920.

17. Schönheimer, R.: Ueber eine eigenartige Störung des Kohlehydrat-Stoffwechsels, Ztschr. f. physiol. Chem. **182**:148, 1929.

18. Exchaquet, L.: Infantilisme hepatique familial, Arch. de méd. d. enf. **34**: 657, 1931.

All three cases occurred in one family; in an older boy, aged 12 years, and in twins, a boy and a girl, aged 3 years. They presented the following characteristics: a large liver since birth, underdevelopment, acetonuria and a normal blood sugar during fasting. The curve for sugar tolerance was abnormal in all three cases and in one case was similar to a diabetic curve. Because of the presence of urobilin and urobilinogen in the urine and because of the increase of uric acid in the blood, cirrhosis of the liver cannot be excluded. Tests with the sugars for function of the liver, however, gave negative results. Should these cases eventually be found to belong to our group, they would be of extreme importance from an etiologic point of view, because of their familial nature.

A number of theories have been propounded as to the etiology of the symptom complex. Schönheimer found that the glycolytic power of the liver in von Gierke's first case was completely lacking, as demonstrated by the fact that after six days there was no decrease in the glycogen of the liver. Because of this, both he and von Gierke postulated that the condition was due to the absence of the glycolytic ferment in the liver. They expressed the belief that the cells of the liver and kidney had lost the power of liberating glycogen but had retained the power of forming and storing it, and that this disturbance was of congenital origin. Van Creveld also believes that the explanation may be found in a disturbance in the action of the glycolytic ferment. Bäumer and Loeschke [19] support this idea and feel that the deficiency of glycolytic ferment may occur in a number of organs, and on this basis explain the tremendous deposit of glycogen in the heart of Bischoff's patient.

Unshelm found an increase in the amylase of the liver; no decrease in the glycogen of the liver after seven days and a marked glycogenolysis when amylase from another liver was added to the liver of his patient. On the basis of these findings, he came to the conclusion that there was an abnormally strong attachment or chemical union between glycogen and protein which prevented glycogenolysis.

Another etiologic factor not considered by these authors is that first mentioned by Priesel and Wagner. In view of the fact that six years after Wagner and Parnas described their case the child became truly diabetic, Priesel and Wagner felt that from the very beginning there may have been a disturbance in the internal secretion of the pancreas. Unshelm found a few abnormal islands in the pancreas in his patient.

The disturbance in the glycogen metabolism in these cases as evidenced by the excessive deposit of glycogen within the cells of the vari-

19. Bäumer, H., and Loeschke, A.: Zum Stoffwechsel bei der Glykogen-Speicherungskrankheit, Klin. Wchnschr. **11**:1824, 1932.

ous organs resembles somewhat the disturbance in lipoid metabolism found in the Gaucher, Niemann-Pick group.

How glycogen and amylase can be found together in the cells of the liver without the occurrence of glycogenolysis has always been a puzzle. Lesser [20] propounded the theory that the two substances are held in separate compartments, and that when a disturbance in the colloidal state of the liver cell occurs, such as results from a change in the tissue hydrogen ion concentration, the amylase is liberated, causing glycogenolysis. It is therefore conceivable that the excessive deposit of glycogen within the liver cells may interfere with the normal glycolytic function of these cells by disturbing the colloidal relationships.

Bäumer and Loeschke consider the liver to be the source of the excess amylase in the urine, but give no explanation for this. The liver, however, is not the only source of amylase. Amylase is also secreted by the salivary glands and the pancreas. We cannot state definitely the origin of the urinary amylase or its interpretation. However, King [21] has shown that in animals the concentration of amylase in the urine can exceed that in the blood, depending on the permeability of the kidney cells. Rosenthal [22] found a diminished excretion of amylase in diabetes insipidus and chronic nephritis and an increased excretion in acute infections. On the bases of these findings, there may be an increased permeability of the kidney cells to amylase in this disease.

COURSE AND PROGNOSIS

We can say very little as to the course of the disease. Van Creveld's patient has been observed over a number of years and has improved; the liver has become smaller, and the blood sugar has assumed a higher level. Neither Loeschke's patient nor ours has been followed long enough to permit conclusions to be drawn. As stated previously, true diabetes mellitus developed in Wagner and Parnas' case. This patient is now 20 years old and is markedly underdeveloped.[23] Intercurrent infections were the cause of death in four cases.

SUMMARY

We have described a case of hepatomegaly based probably on a disturbance in the glycogen metabolism. The cardinal symptoms are

20. Lesser, E. J.: Räumliche Trennung von Glykogen und Diastase in der Leberzellen, Biochem. Ztschr. **119**:108, 1921.

21. King, C. E.: Studies on Blood and Urinary Amylase, Am. J. Physiol. **35**: 301, 1914.

22. Rosenthal, A.: Zur Frage der Ausscheidung von diastatischem Ferment im Urin, Deutsche med. Wchnschr. **37**:923, 1911.

23. Personal communication.

enlarged liver, hypoglycemia, acetonuria, increased urinary amylase and underdevelopment. We have reviewed the literature and have presented the various theories as to the pathogenesis.

NOTE.—Since this paper was submitted for publication, the patient has been in the hospital for a third time. The only new positive finding is the fact that lipemia has developed, the total blood fat on fasting being 2.3 per cent on one occasion and 3.4 per cent on another. Likewise, Baumer and Loeschke [24] have reported the development of a lipemia in their case.

Not included in our paper is the article by Schall,[25] who in December, 1932, published the reports of three cases of the disease, which we are describing; in one of these cases the diagnosis was confirmed by biopsy.

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24. Baumer, H., and Loeschke, A.: Zum Stoffwechsel und zur Differentialdiagnose der Glykogenspeicherkrankheit, München. med. Wchnschr. **80**:377, 1933.

25. Schall, L.: 3 Falle von Glykogen-Speicherkrankheit (Hepatomegalia Glykogenica von Gierke), München. med. Wchnschr. **79**:2079, 1932.

MULTIPLE MYELOMA IN A CHILD

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Multiple myeloma may be defined as a primary malignant tumor of bone marrow characterized by multiple foci in long and flat bones of the skeleton and usually associated with anemia, Bence-Jones proteinuria, rare metastasis and a fatal termination. MacIntyre [1] described the condition in 1850, but von Rustizky [2] first recognized it as a specific disease of the bone marrow, and referred to it as myeloma. Kahler,[3] in 1889, called attention to the associated proteinuria, hence the reference in the literature to "Kahler's disease." Geschickter and Copeland,[4] in 1927, reviewed 425 cases from the literature, and stated that multiple myeloma was present in only 0.03 per cent of all malignant conditions. Symmers [5] found only three cases of the condition in the course of 6,000 postmortem examinations performed at Bellevue Hospital, New York City. Thus the rarity of multiple myeloma is evident.

The disease usually afflicts persons well past middle age, with the peak at 55 years, and in their series of cases Geschickter and Copeland [4] found only five patients less than 35 years of age; in two the condition was not proved microscopically. A search of the literature has revealed few authentic cases occurring in childhood.

Cases reported by Roman,[6] and de Elizalde and Llambias [7] are not considered to have been cases of myeloma. Gilmore's [8] case was accepted as one of myeloma, with dissension by Bloodgood, Mallory and Wolbach.[9] Two cases reported by Berkheiser,[10] in 1924, resembled Chris-

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Read before the Northwestern Pediatric Society, Rochester, Minn., on Nov. 4, 1932.

1. MacIntyre, William: Case of Mollities and Fragilitas Ossium, Tr. Med.-Chir. Soc. Edinburgh **33**:211, 1850.
2. von Rustizky, J.: Multiples Myelom, Deutsche Ztschr. f. Chir. **3**:162, 1873.
3. Kahler, quoted by Geschickter and Copeland.[12]
4. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. **16**:807 (April) 1928.
5. Symmers, Douglas: The Multiple Myelomata and Their Ability to Metastasize, Ann. Surg. **67**:687 (June) 1918.
6. Roman, quoted by Geschickter and Copeland.[4]
7. de Elizalde and Llambias, quoted by Geschickter and Copeland.[4]
8. Gilmore, M. E.: Multiple Myeloma Syndrome in a Child, Texas State J. Med. **21**:358 (Oct.) 1925.
9. Bloodgood, Mallory and Wolbach, quoted by Geschickter and Copeland.[4]
10. Berkheiser, E. J.: Multiple Myelomas of Children, Arch. Surg. **8**:853 (May) 1924.

tian's disease in one instance and Ewing's endothelial myeloma in the other. In 1930, Jacoby [11] reported the case of a child aged 8 years; the diagnosis was proved at necropsy and multiple involvement of the vertebrae was revealed. Zäh,[12] in 1932, reported what he asserted was the first authentic case of multiple myeloma in childhood to be reported in Germany and the third to be reported in the world. In this case, metastatic growths were found in the lungs. The cases presented by Gilmore, Jacoby and Zäh were substantiated as instances of multiple myeloma by microscopic evidence, whereas the other cases reported as occurring in childhood subsequently have been found to be instances of other conditions or histologic evidence to support the diagnosis [4] has been lacking. The extreme rarity of the disease and the doubt regarding its occurrence in childhood have been kept in mind in submitting the report of the case as an instance of multiple myeloma in a child.

Characteristic recurrent pain is the predominant symptom in this disease, with exacerbations and remissions. Geschickter and Copeland [13] analyzed the various complaints of patients in their large series, and noted that gastro-intestinal symptoms such as abdominal pain, distention and vomiting were found in about 20 per cent of cases. In their series and in a case reported by Meyerding,[14] the gastric disturbances were explained on the basis of compression of the spinal cord by the deformity of the spinal column or by pressure of the tumor. In such cases the picture was that of an acute abdominal condition; this is well illustrated in the following case which was studied with the counsel of Dr. R. L. J. Kennedy.

REPORT OF A CASE

History.—A white boy, aged 4 years, was brought to the Mayo Clinic on Aug. 9, 1932, because of recurring attacks of abdominal pain of one year's duration. The boy was born in Minnesota of German-American parents. The family history and the past history were essentially negative. His development was normal. He was well until September, 1931, when, following an attack which was characterized by abdominal distention and rigidity and slight fever, he fainted, remaining unconscious for several minutes. The symptoms persisted for several hours and were relieved by an enema; the patient entirely recovered on the following day. Three months later, after obstipation for four days, he suffered a similar attack with pain in the right lower quadrant of the abdomen, which was relieved again by an enema. Then followed a period of quiescence until February, 1932, when he began

11. Jacoby, Paul: Myelomatosis in a Child of 8 Years, Acta radiol. **11**:224, 1930.

12. Zäh, Karl: Ueber Myelom im kindlichen Alter, Virchows Arch. f. path. Anat. **283**:310, 1932.

13. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, New York, Am. J. Cancer, 1931, p. 430.

14. Meyerding, H. W.: Multiple Myeloma, Radiology **5**:132 (Aug.) 1925.

complaining of pain in the right lower quadrant of the abdomen when playing, and an attack similar to the others occurred. From this time on, attacks were precipitated by slight falls or exertion.

In April an attack was diagnosed as being caused by appendicitis, and appendectomy was performed elsewhere. The patient's mother said that she had been informed that "no abnormalities were found but the appendix was kinked and beginning to form pus." After the boy had felt well for two weeks, the abdominal pain and distention recurred every two or three weeks. On August 1, he had

Fig. 1.—*A,* anteroposterior view, showing mottling and rarefaction of the pelvic bones, Aug. 9, 1932. *B,* lateral view of a lumbar portion of the spinal column and of the pelvis, Aug. 9, 1932; deformity of the first and second lumbar vertebrae due to compression may be noted.

"stomach flu" with a temperature of from 102 to 104 F., but no vomiting or diarrhea. He complained of pains in the legs, and after he had been in bed for several days his weakness was so marked that he was unable to stand or walk. He also complained of pain in the abdomen, which was accentuated by straining or effort of any slight degree. At this time he was brought to the clinic.

Examination.—Physical examination revealed a thin, pale boy, whose height was 40 inches (101 cm.) and weight 29½ pounds (about 13 Kg.). The average weight for a child of his height is 36 pounds (about 16 Kg.). The pulse rate

was 100 beats a minute, and the oral temperature, 98.6 F. Carious teeth, cervical adenopathy and enlarged tonsils were noted. There was a scar in the right lower quadrant of the abdomen. The patellar reflex was hyperactive, but the cremasteric and epigastric reflexes were not elicited. There was localized tenderness over the middle lumbar spines. The results of examination were otherwise essentially negative.

Repeated urinalyses gave negative results except for a trace of albumin on several occasions. The Bence-Jones reaction was absent on a number of examinations. Erythrocytes numbered 4,150,000, and leukocytes, 5,300 per cubic millimeter of blood; the value for hemoglobin was 11.1 Gm. per hundred cubic centimeters of blood (66 per cent). The differential count was normal. Blood smears disclosed slight anisocytosis, poikilocytosis and polychromatophilia. The Wassermann test of the blood and the Mantoux test both gave negative results. The

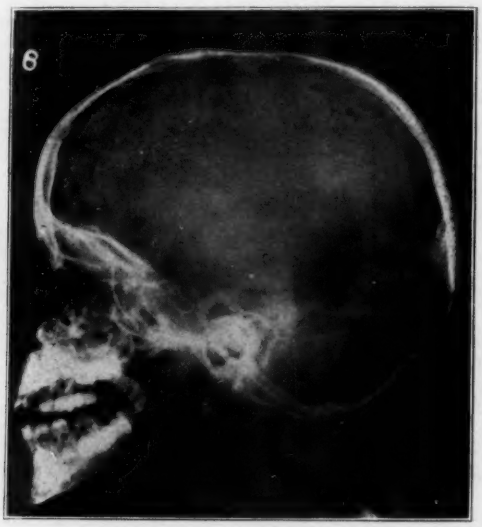

Fig. 2.—Lateral view of the skull, disclosing evidence of multiple punched-out areas where destruction of the bone has taken place.

value for serum calcium was 9.2 mg., and the value for serum phosphorus, 4.7 mg., per hundred cubic centimeters. A roentgenogram of the thorax showed nothing abnormal. Roentgenograms of the hips and lumbosacral portion of the spinal column showed a compression deformity of the first and second lumbar vertebrae. There was irregular mottling of the bones of the pelvis with symmetrical areas of rarefaction in each acetabulum (fig. 1). A roentgenogram of the skull revealed multiple regions of destruction throughout (fig. 2).

In view of the results of examination, the diagnosis of multiple myeloma was made, and the child was sent home.

Course.—On August 17, the patient was admitted to the hospital, acutely ill. There was a history of constipation, fever, abdominal pain and vomiting for two days. Enemas had been unsuccessful. The child complained of pain in the abdomen. The temperature was 102.8 F., and the pulse rate 136 beats a minute. The blood pressure in millimeters of mercury was 96 systolic and 72 diastolic. The findings were as previously noted, with the following additions: There was no visible

peristalsis or distention. Tenderness and rigidity were present in the lower part of the hypogastrium and in the left lower quadrant of the abdomen. No masses or viscera were felt, and the genitalia were normal. There was no hernia. The spinal column presented localized points of tenderness from the twelfth thoracic to the first sacral segment. The patient complained of pain on moving the head and protected his back during the examination. On being moved, he complained of pain in the middle lumbar region. Leukocytes numbered 24,000 per cubic millimeter of blood; the percentages of the various types of leukocytes were as follows: polymorphonuclears, 81; monocytes, 6, and lymphocytes, 13.

The diagnosis was not clear, as the picture simulated an acute abdominal condition, particularly acute intestinal obstruction. However, in view of the previous history of recurrent similar attacks, the localized tenderness over the spinal column

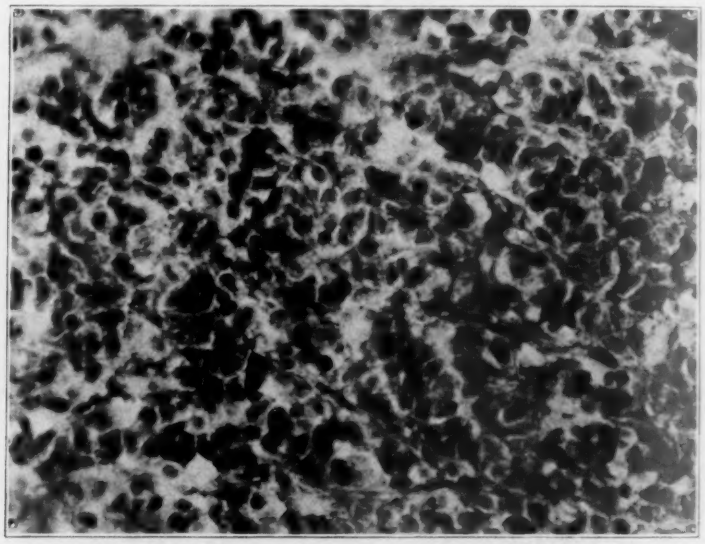

Fig. 3.—Tumor tissue taken from the skull for biopsy (× 400).

and the previous positive roentgenograms, pain in the nerve roots was considered to be the cause of the signs and symptoms. After a few days the tenderness of the abdomen became less marked, the general condition improved, and the leukocyte count and the temperature returned to normal. The child was comfortable.

On August 27, a specimen for biopsy was removed from the right parietal bone of the skull; it contained two nodules. The pathologist reported that a section of the specimen revealed myeloma (fig. 3). Palliative roentgen therapy was applied to the skull and spinal column, following which the patient was dismissed, but he was instructed to return for reexamination.

On October 7, a note was received from the patient's mother, stating that his general condition was greatly improved, but that he complained of pain in the right leg and the abdomen on moving or creeping; walking was not possible.

The child was brought to the clinic again on November 28. Since his previous dismissal, he had complained almost continually of pain in the lower part of the thorax, in the upper and lower parts of the abdomen and in the right leg. He had been bedridden, for he was unable to creep, walk or stand on account of the pain.

His appetite was much poorer, and he seemed to be failing rapidly. In addition to the previous findings, examinations revealed kyphosis of the first to the third lumbar vertebrae and a pigeon-breast deformity of the lower part of the sternum. He complained of pain when touched. There was a suggestion of ankle clonus, but the reflexes were intact. The spine was held rigidly in a markedly kyphotic position.

Urinalysis was again negative for Bence-Jones bodies, and the number of erythrocytes and the concentration of hemoglobin were essentially unchanged. Leukocytes numbered 3,400 per cubic millimeter, and the value for urea was 28 mg.

Fig. 4.—*A,* anteroposterior view, taken on June 1, 1933, showing greatly increased destruction and rarefaction of the vertebral bodies and the pelvic bones. *B,* lateral view, taken on May 31, showing increased deformity of the lumbar vertebral bodies. This is to be compared with figure 1 *B.*

per hundred cubic centimeters of blood. A roentgenogram of the spinal column, taken on November 28, revealed a compression deformity of the third to the fifth thoracic vertebrae and an increase of the lumbar deformity previously noted. The entire spinal column showed evidence of great destruction. Kyphosis and scoliosis were also present. There was generalized mottling of the pelvic bones to an extent greater than before.

The pains in the thorax and in the upper part of the abdomen might be accounted for by the deformity of the thoracic vertebrae, with resulting compression of the

spine and nerve roots. On this admission it was evident that the child was declining rapidly, as the symptoms and the physical signs were greatly aggravated.

The patient was given further roentgen irradiation to the spinal column and skull in an effort to relieve the pain.

Although the boy was free from pain for a short period early in 1933, he became progressively weaker, with increasing pallor and pain in the back and extremities. The retrogression continued, despite repeated doses of roentgen rays in an attempt to ameliorate the excruciating pain that incapacitated him. When he was seen at the clinic on May 31, 1933, on his last admission, it became neces-

Fig. 5.—Lateral view of the skull, taken on June 1, revealing greater involvement of the bone. The area of biopsy is evident. This roentgenogram is to be compared with figure 2.

sary to resort to morphine in order to give him rest. He had lost considerable weight, and roentgenographic examination at the time revealed greatly increased destruction of the vertebral bodies; the pelvic bones and the skull were more extensively involved with tumor (figs. 4 and 5). The clinical diagnoses recorded were: multiple myeloma with nerve root pain, secondary anemia, exhaustion, dental caries, cervical adenopathy and malnutrition. The child died suddenly, at home, on June 29, and postmortem examination was performed the following day by Dr. D. C. Beaver (section on pathologic anatomy, the Mayo Clinic) to whom I am indebted for the necropsy observations.

Necropsy.—The embalmed body was 102 cm. in length, and its estimated weight was from 25 to 30 pounds (11.3 to 13.6 Kg.). Emaciation was marked. No edema, cyanosis or jaundice was present. Multiple noninfected scratches and deep abrasions were noted over the forehead, skull and thorax. A decubital ulcer, 1 cm. in diameter, was observed in the sacral region. The hair of the head was almost entirely gone.

The thymus weighed about 2 Gm. and was almost completely atrophied.

The heart weighed 140 Gm. No epicardial fat was present. The muscle was light pink. All the chambers, particularly the left ventricle, were dilated. The heart was normal in other respects.

The right lung was grayish pink, and lobular markings were prominent. Throughout all portions, but particularly in the upper lobe and upper portions of the lower lobe, were hemorrhagic patches of increased consistency. Crepitation was increased in other portions of the lung. The cut surface seemed normal except for the patches of consolidation, which had a grayish, hemorrhagic appearance. In the consolidated portions, the amount of frothy fluid was increased. No regions of tumor were found.

The left lung corresponded in all respects to the right lung.

The spleen weighed 325 Gm. (normal, 53 Gm.). Its consistency was increased, and its color was grayish pink. The capsule was smooth and glistening. The cut surface revealed the same color, with grayish portions consisting of indefinitely small nodules. Normal malpighian markings and trabeculations were replaced by the grayish-pink transformation. No definite regions of tumor were found.

The liver weighed 600 Gm., and appeared normal. The capsule was smooth and glistening, and the consistency, firm and rubbery. No tumor masses were found. The gallbladder, ducts and portal vein were normal.

The kidneys were normal. Each weighed 75 Gm. and presented fetal lobulation. The ureters, urinary bladder, prostate gland and genitalia were normal.

The lymph nodes of the hilar, peribronchial and peritracheal regions were slightly enlarged and grayish. No evidence of tuberculosis was found.

Examination of the skull was made through a small cerebellar incision, beneath which bone was chiseled away. There seemed to be a thinning of the inner and outer tables, with thickening of the medullary substance, which was patchy in distribution. To transmitted light the thickened areas appeared dark and the normal areas light. The thickened medullary substance was hemorrhagic, with a grayish hue.

The vertebrae were examined from the third thoracic segment to the sacrum. There was erosion of the bodies of the vertebrae, with increase of what seemed to be marrow substance. The marrow was grayish and hemorrhagic, and in some places, particularly in the last lumbar vertebra, there were definite hemorrhagic foci which appeared like tumor. The bodies of the vertebrae were markedly narrowed, especially the last thoracic and first lumbar segments. All the vertebrae were thinned. The disks were prominent, and central gelatinous portions were present.

Sections of the left ilium revealed changes similar to those in the bones of the skull.

Examination of the right femur, from the head to the middle third, revealed no change in the shaft, but the marrow substance had a peculiar, grayish hemorrhagic, mostly fatty appearance. As the head of the bone was approached, the marrow substance seemed to be definitely increased. The cortex of the bone was decreased and seemed infiltrated with the same material as that seen in the marrow. The

cancellous bone in the head of the femur was softer than normal, and the marrow was increased, having the consistency of soft tumor substance. The bone was friable and fleshy.

Examination of the ribs revealed no visible changes. Other structures which were grossly normal and which have not been named elsewhere were the peritoneum, pleura, pericardium, esophagus, stomach, duodenum, intestinal tract, pancreas, suprarenal glands and aorta.

Microscopic examination disclosed significant features. There were marked congestion of the lungs and exudation of serum into the alveoli in places. Only a few leukocytes were seen. The alveolar walls were intact. No tumor cells

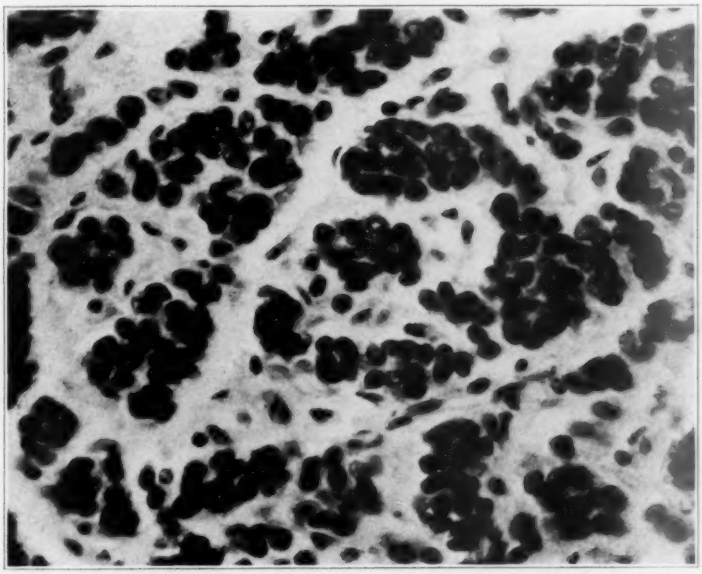

Fig. 6.—Section of the tumor tissue from the bone marrow of the head of the right femur (× 500).

were seen. Sections of the heart muscle revealed an extreme degree of lipoid degeneration. The thymus gave evidence of marked atrophy and involution. In the lumens of the majority of the renal tubules there was a granular accumulation. No fat or tumor tissue was noted.

Sections of the bone marrow from the upper end of the right femur revealed tumor cells arranged in a manner suggesting cords or columns. The tumor had practically replaced the normal marrow but had not obliterated the fat tissue. In many instances, it occupied the septums separating the fat cells. The cells were of the myeloblastic type, with centrally situated nuclei and a small amount of rather eosinophilic cytoplasm. The nuclei were mostly hyperchromatic. Mitotic figures were present but not in large numbers. Plasma cells were not encountered. In some portions the tumor elements preponderated, whereas in other places there were relatively few tumor cells scattered throughout the marrow (fig. 6).

Sections of cancellous bone from the head of the right femur presented essentially the same features as those noted in the marrow.

The marrow of the vertebral bodies was necrotic.

There was slight, patchy infiltration of the liver with tumor cells, chiefly adjacent to the portal spaces. There was apparently some hyperplasia of the duct cells in these localities, so that both duct and tumor cells made up the regions of infiltration. In addition, there was moderate hydropic degeneration of the hepatic cells (fig. 7 *A*).

The normal structure of the spleen was entirely lost, and the splenic pulp was almost entirely replaced by tumor cells, with only the arterioles of the malpighian

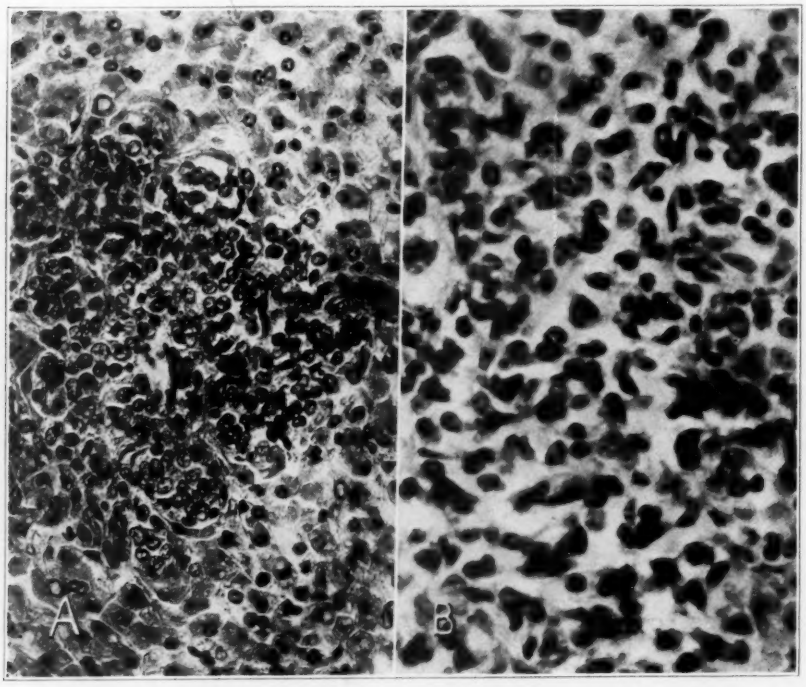

Fig. 7.—*A*, involvement of the liver by the tumor (× 300). *B*, section of the spleen, showing the replacement of the normal tissue by the tumor (× 500).

corpuscles remaining. Lymphocytic tissue and sinus spaces were completely replaced by tumor cells. These presented large nuclei and scanty, eosinophilic cytoplasm. Few eosinophils were noted apart from the tumor cells. The growth in the spleen was diffuse, rather than being in cords or columns, as was noted in the bone marrow of the femur. The type of cell was essentially the same as that of the bone marrow. Few mitotic figures were seen (fig. 7 *B*).

Sections taken from the peribronchial, peritracheal, cervical and mesenteric lymph nodes presented a hyperplastic reaction of the reticulo-endothelium with atrophy of the lymph follicles. In one node taken from the aortic region, tumor cells were noted which varied markedly in size and shape, but the same general characteristics that were noted in the other regions were maintained.

The suprarenal glands, the prostate gland, the parathyroid glands, the thyroid gland and the pancreas were normal.

Anatomic diagnoses were as follows: multiple myeloma (resembling the myeloblastic type) of the skull, vertebrae, ilium, right femur and other structures; involvement with tumor of the spleen, liver and aortic lymph nodes; hemorrhagic edema of the lungs; dilatation of the heart and fatty changes of the myocardium; secondary anemia with exhaustion (clinical); decubital ulcer; self-inflicted abrasions and alopecia.

COMMENT

In this case there was gradual decline, despite slight remissions, to a fatal termination. The history, roentgenologic findings and necropsy point to the diagnosis of multiple myeloma.

When the child was admitted to the hospital for the second time, the picture of an acute abdominal condition presented itself, but the previous history, the localized tenderness of the spinal column, the roentgenographic observations and the report of biopsy suggested the probability that the nerve root pain accounted for the clinical picture that simulated a surgical emergency.

Although MacCallum [15] has asserted that multiple myeloma appears only in bone marrow, there are many opinions to substantiate the belief that the presence of visceral involvement is not inconsistent with the diagnosis. Involvement of the liver and the spleen with tumor masses identical with those found in the bone marrow has been reported in the literature. The spleen has been reported as a site of metastasis by Arnold,[16] Aschoff,[17] Askanazy [18] and Reach.[19] Hoffman,[20] Mieremet,[21] Scheele and Herxheimer,[22] Shennan [23] and Arnold have reported metastasis in the liver. Growths have been found in the lymph nodes by

15. MacCallum, W. G.: A Text-Book of Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1932.

16. Arnold, quoted by Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1932.

17. Aschoff, L.: Ein Fall von Myelom, München. med. Wchnschr. **53**:337, 1906.

18. Askanazy, S.: Ueber die diagnostische Bedeutung der Ausscheidung des Bence-Jones'schen Körpers durch den Harn, Deutsches Arch. f. klin. Med. **68**:34 (Aug. 16) 1900.

19. Reach, Felix: Ein Beitrag zur Kenntnis der Bence-Jones'schen Albuminurie, Deutsches Arch. f. klin. Med. **82**:390 (Feb. 2) 1905.

20. Hoffman, Rudolf: Ueber das Myelom mit besonderer Berücksichtigung des malignen Plasmoms, Beitr. z. path. Anat. u. z. allg. Path. **35**:317, 1904.

21. Mieremet, C. W. G.: Ueber "Systemerkrankung" und Tumorbildung der blutbereitenden Organe, Virchows Arch. f. path. Anat. **219**:1 (Feb. 4) 1915.

22. Scheele and Herxheimer: Ueber einen bemerkenswerthen Fall von multiplem Myelom, Ztschr. f. klin. Med. **54**:57, 1904.

23. Shennan, Theodore: Multiple Myeloma and Its Association with Bence-Jones' Albumose in the Urine, Edinburgh M. J. **10**:321 (April) 1913.

Arnold, Christian,[24] Lubarsch,[25] and Charles and Sanguinetti.[26] Thus, there is ample evidence that visceral involvement may occur in multiple myeloma.

Nicholls [27] quoted Adami in stating that in uncomplicated cases there is no metastasis, but occasionally an individual mass may take on malignant infiltrative properties, and when this is the case, secondary growths of sarcomatous type may be found in other organs. Nicholls suggested that the development of secondary growths may be evidence of compensatory myelogenous activity on the part of the tissue when the function of the bone marrow is disturbed. Lubarsch sought to explain growths in the liver and spleen as independent rather than metastatic nodules in the hematopoietic tissue. However, the finding of tumor cells in blood vessels by Abrikossoff [28] and others [29] accounts for metastasis. Tumor cells circulating in the blood in cases of multiple myeloma have been reported by Beck and McClearly [30] and by Aschoff. Scott, Stanton and Oliver [31] found myeloma plasma cells diffusely distributed in the sinusoids of the liver and in the capillaries of the kidney in one of their cases. This seems to point to metastatic dissemination, but Hoffman, Heilmann,[32] Barr [33] and others regarded multiple myeloma as a systemic disease of hematopoietic organs and did not think that visceral involvement was evidence of true metastasis. Nicholls' case of primary plasma cell tumor of the vertebrae and the ribs, with secondary nodules of similar nature in the pleura, peritoneum, peribronchial and mesenteric lymph nodes, heart, lungs, spleen, intestines, liver, pancreas, ovaries, uterus, spinal cord and skin, is certainly evidence in favor of metastatic dissemination. Symmers' case revealed tumor tissue in the perisuprarenal fat, and he cited Christian's case, in which the soft

24. Christian, H. A.: Multiple Myeloma: A Histological Comparison of Six Cases, J. Exper. Med. **9**:325 (July 11) 1907.

25. Lubarsch, O.: Zur Myelomfrage, Virchows Arch. f. path. Anat. **184**:213 (May 11) 1906.

26. Charles, J. R., and Sanguinetti, H. H.: Multiple Myeloma, Brit. M. J. **1**:196 (Jan. 26) 1907.

27. Nicholls, A. G.: Multiple Myeloma of Unusual Type with Widely Disseminated Metastases of Small Type, Canad. M. A. J. **17**:301 (March) 1927.

28. Abrikossoff, A. J.: Ueber einen Fall von multiplem Myelom mit diffuser Verbreitung im Knochenmark, Virchows Arch. f. path. Anat. **173**:335 (Aug.) 1903.

29. Hoffman [20] and Shennan.[23]

30. Beck, H. G., and McCleary, Standish: Multiple Myeloma with Bone Marrow Plasma Cells in the Blood, J. A. M. A. **72**:480 (Feb. 15) 1919.

31. Scott, Ernest; Stanton, F. M., and Oliver, Mary: Multiple Myeloma, Am. J. Cancer **17**:682 (March) 1933.

32. Heilmann, P.: Zur Myelomfrage, Beitr. z. path. Anat. u. z. Allg. Path. **80**:652, 1928.

33. Barr, D. P.: Multiple Myeloma, Ann. Int. Med. **1**:884 (May) 1928.

tissue of the arm was involved with tumor. These seemed instances of metastasis, but Symmers remarked that since the liver, spleen and lymph nodes are hematopoietic tissues in the embryo, myeloblastic tumors might arise from them independently of the bone marrow. Symmers also cited the case of Pepper and Pearce, in which the spleen was diffusely infiltrated with tumor cells, as it was in my case. The question regarding the origin of visceral tumors in this disease is unsettled, but from the evidence submitted one may definitely conclude that visceral involvement may occur in multiple myeloma.

The etiologic factors of trauma, infection and irritation have been suggested but there is no evidence to support these hypotheses. The symptoms of the disease are varied, but Geschickter and Copeland [4] suggested six cardinal signs and symptoms: (1) multiple involvement of the skeletal trunk, (2) pathologic fracture, (3) Bence-Jones proteinuria in from 65 to 70 per cent of the cases, (4) characteristic backache with early signs of paraplegia, (5) inexplicable anemia and (6) chronic nephritis, retention of nitrogen and hypertension.

In the case reported, the anemia became progressively worse, and Bence-Jones proteinuria was never found. Boggs and Guthrie [34] reviewed the literature and noted albumosuria in a multiplicity of diseases, including osteomalacia, gunshot wound of the leg, myxedema, lymphatic leukemia, chloroma and metastatic carcinoma. However, they found reports of cases of epiphysitis, arthritis, rachitis, pernicious anemia, lead poisoning and myeloma in which there was widespread involvement of the bone marrow but no Bence-Jones proteinuria. Thus Bence-Jones proteinuria is not specific for multiple myeloma, although it is found in from 65 to 70 per cent of the cases.

Several conditions might be confused with multiple myeloma; they should be considered in the differential diagnosis. Hyperparathyroidism tends to present generalized and diffuse osteoporosis of the skeleton, whereas in multiple myeloma the regions of destruction of bone are isolated, and the generalized osteoporosis is lacking, as noted particularly in the skull. Also, the parathyroid glands are normal, as was noted in this case. In late stages of the disease there is a tendency to formation of cysts of the parathyroid glands, with an increased value for serum calcium; in the case presented, however, this value was normal. Tuberculosis of the bone may be ruled out by the negative tuberculin test and by the presence of a multiplicity of lesions of the bone. Christian-Schüller's syndrome characteristically includes exophthalmos, xanthomatosis, formation of cysts and diabetes insipidus; moreover, the condition is of much longer duration. These features are usually lacking

34. Boggs, T. R., and Guthrie, C. G.: The Bence-Jones Proteinuria in Conditions Other Than Myelomatosis, Bull. Johns Hopkins Hosp. **23**:353 (Dec.) 1912.

in multiple myeloma. Ewing's [35] tumor is a single lesion which may be designated as both myelo-endothelioma and myeloma, and although the pathologic appearance may be similar to that found in multiple myeloma, the distinction is made on the basis of clinical and roentgenologic features and the lack of response of multiple myeloma to roentgen therapy. Chloroma is a myeloblastic cell tumor, usually recognizable by its green color and by the blood picture. Osteomalacia is not likely to cause confusion, for it lacks the destructive features of myeloma and is marked, instead, by softening and resulting deformity of the bones due to diffuse absorption of lime. Hodgkin's disease lacks the clinical history, roentgenologic features and microscopic picture of myeloma. Metastatic carcinoma presents a roentgenologic shadow that is moth-eaten in appearance and lacks the usual clearcut features of myeloma.[14] The diagnosis of multiple myeloma rests on the clinical history, roentgenogrophic features and biopsy or necropsy, and the symptoms depend on the regions involved by the tumor.

The histologic findings in the disease are variable, and there is a diversity of opinion regarding the identity of the type cell. This cell may resemble the plasma cell or the myelocyte, but the intermediary forms are frequently encountered. Ewing has classified the tumor as (1) plasmacytoma, (2) erythroblastoma, (3) lymphoblastoma and (4) myelocytoma, depending on the characteristics of the predominant cell. Symmers expressed the opinion that the cell is a plasma cell of bone marrow indistinguishable from the myeloblast, and stated that the myeloblast is the only cell from which it is possible for a genuine myeloma to spring. Vance [36] said that there were still uncertainty and lack of unanimity in regard to the true classification of the tumors, although most pathologists agree that they are derived from blood-forming cells of the bone marrow and are related to the primary diseases of the lymphatico-hematopoietic apparatus. He also noted that five different types of multiple myelomas have been distinguished in the literature, on the basis of the morphology of the tumor cell, as to whether it resembles (1) the myeloblast, (2) the small lymphocyte, (3) the neutrophilic myelocyte, (4) the erythroblast or (5) the plasma cell. Vance also pointed out that the myeloblastoma is the only multiple myeloma recognized as a pathologic entity, and the term "multiple myeloma" should be reserved for multiple tumors of the bone marrow of myeloblastic origin, because the other types may resemble other entities. In a study of six cases, Christian noted striking similarity of the cell structure, with minor differences; for the most part the cells

35. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

36. Vance, B. M.: A Case of Multiple Myeloma with a Discussion as to Its Nature and Origin, Am. J. M. Sc. **152**:693 (Nov.) 1916.

resembled plasma cells. Wallgren [37] expressed the belief that the type cell is transitional. The question is still unsettled, and suggests the need for more exact classification, for the term "multiple myeloma" embraces too many histologic variations, even though the clinical and roentgenologic pictures are usually similar. Many observers would adhere narrowly to certain general clinical characteristics. Winkler [38] insisted on a strict limitation of the process to the bone marrow, absence of metastasis, the importance of albumosuria, and the perfectly uniform size and character of the cells. However, as Lubarsch has pointed out, the metastasis is accidental, the albumosuria may be absent, and the size and form of the cells may vary considerably in cases which in general give the impression of essentially the same disease. MacCallum [39] stated that the tumors are distinguishable from other tumors by the mode of growth and the absence of metastasis, and from myelogenic sarcomas by their multiplicity, the uniformity of their component cells and the fact that giant cells and spindle cells are practically absent. Whether the condition should be classified as of four types or whether it is one of varying grades of anaplasia in a single cell is still undetermined, but according to Ewing the former view seems to be in favor at present.

Treatment of this condition is palliative and consists of measures to improve the general condition, rest to prevent pathologic fractures and high voltage roentgen therapy in an attempt to allay the pain.

The prognosis is hopeless, as patients do not live more than two years. Geschickter and Copeland,[12] however, reported that one patient lived for five and a half years. The patient in the case presented lived twenty-one months from the onset of the symptoms.

SUMMARY

A survey of the literature reveals the extreme rarity of multiple myeloma in childhood.

A case encountered at the Mayo Clinic involved a child, aged 4 years, with characteristic findings and involvement of the spleen, liver and aortic lymph nodes.

37. Wallgren, Avrid: Untersuchungen über die Myelomkrankheit, Upsala läkaref. förh. **25**:113, 1920.

38. Winkler, K., quoted by Ewing.[35]

39. MacCallum, W. G.: A Case of Multiple Myeloma, J. Exper. Med. **6**:53, 1901-1905.

Progress in Pediatrics

NONTYPHOID CHOLECYSTITIS IN CHILDHOOD

WITH THE REPORT OF AN UNUSUAL CASE WITH CHOLANGEITIS

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Disease of the gallbladder in children has received little attention from the medical profession at large. Textbooks tend to ignore the subject or to dismiss it with curt remarks.[1] Yet the literature presents about 300 of these cases. In 1898 Mendel [2] analyzed 16 cases of cholelithiasis observed by him in children under 8 years of age. The next year Still [3] recorded 20 cases of biliary calculus in childhood appearing in the literature from the time of Gibson in 1722. He added 3 more cases in which the diagnosis was proved. During the following two decades only isolated case studies appeared. In 1920 Reid and Montgomery [4] collected 18 cases of typhoid fever in children under 15 years of age who had died or had been operated on because of disease of the gallbladder. In 1923 Kellogg [5] presented in tabular form 64 cases recorded in a two hundred year period. A little later, Graff was given credit [6a] for collecting from the literature 25 cases of acute cholecystitis without stones, and Grekov was credited [6] with having collected 77 cases of cholecystitis plus 2 of his own. In June, 1928, Potter [7] made the single largest study, gleaning 226 cases of all types in children under 15 years, and presented them after the manner of Kellogg. The following August, Beals [8] reported similarly 60 cases.

I was particularly interested in going over the literature to find cases which resembled the one reported in this article, that of a boy aged 11 years, who had nontyphoid cholecystitis and no stones. Besides

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From the Children's Medical Service of the Massachusetts General Hospital.

1. (*a*) Montgomery, A. H.: Diseases of the Gallbladder in Children, Am. J. Dis. Child. **44**:372 (Aug.) 1932. (*b*) Snyder, C. C.: Cholecystitis and Cholelithiasis in Young Children, J. A. M. A. **85**:31 (July 4) 1925.

2. Mendel, A. V.: M. Rec. **54**:41, 1898.

3. Still, G.: Tr. Path. Soc. London **50**:151, 1899.

4. Reid, M. R., and Montgomery, J. C.: Bull. Johns Hopkins Hosp. **31**:7, 1920.

5. Kellogg, E. L.: Ann. Surg. **77**:587, 1923.

6. (*a*) Bittner, W.: Arch. f. Kinderh. **95**:158, 1932. (*b*) Muller, W.: Zentralbl. f. Chir. **53**:3092, 1926.

7. Potter, A. H.: Surg., Gynec. & Obst. **46**:795, 1928.

8. Beals, J. A.: South. M. J. **21**:666, 1928.

the case study, the additional purpose of this article was to survey similar cases in children under 15 years of age described in the literature and also in the records of the Massachusetts General Hospital.

REPORT OF CASE

An American schoolboy, aged 11, came to the Massachusetts General Hospital on Aug. 19, 1932, with a chief complaint of intermittent fever for two weeks. Two weeks before, he had returned to his home in Boston from a visit to a nearby town, where he had drunk from a well and had swum in a fresh-water pond. There were no cattle, goats or hogs in this vicinity, and no known typhoid. He had been enjoying perfect health.

The illness began with fatigue, feverishness and vomiting within the first twenty-four hours after his return home. These symptoms subsided as quickly as they had appeared. Two days later the fever recurred, and the patient grew delirious and had a chill. Several days of normal temperature ensued.

About a week before admission the temperature rose rapidly to 104 F.; the appetite was lost, and a mild pain was felt in the right lower quadrant. No nausea,

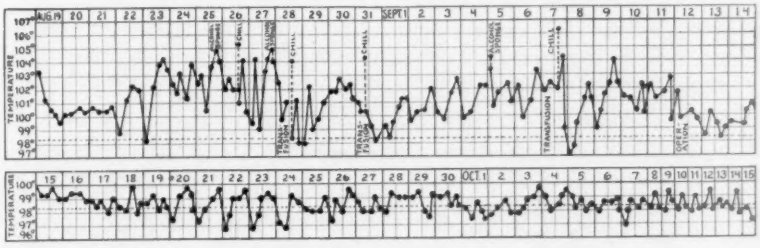

Chart showing variations in temperature of the author's patient during hospitalization.

vomiting or irregularity of the bowels occurred. This attack soon passed, and the patient got up. Four days before admission there were nosebleed and a slight dry cough. Two days before admission the temperature rose for the fourth time (103 F.). The patient vomited for the second time. The bowels functioned normally.

The past history included measles at the age of 5 years, pertussis at 7 and scarlet fever at 9. The family history was not pertinent.

Physical examination disclosed a thin, lanky, pale, apathetic boy, lying quietly in bed. The skin was dry, the nose slightly obstructed, the throat moderately red and the tongue coated. The rectal and ophthalmoscopic examination and all general examinations gave negative findings. The temperature was 103.2 F., the pulse rate 130, the respiration rate 36 and the white blood count 7,000, with 82 per cent polymorphonuclears and 16 per cent lymphocytes.

During the first three weeks in the hospital the chart showed a strikingly hectic fever, with excursions of temperature as great as 15 F. within twenty-four hours. The curves were irregular and were especially pronounced following several spongings and four chills, three of which were associated with reactions following transfusion. During one week the temperature daily topped 104 F., and the pulse rate varied between 130 and 80. Yet the patient showed no local physical signs. He lay indifferently, ate poorly, lost weight and grew paler. A diagnosis had not been made.

A summary of the laboratory data for this period is indicative of the baffling nature of the case.

Urine and Stools.—These were normal, despite repeated cultures for typhoid, paratyphoid and dysentery bacilli.

Blood.—The white blood count rose from 7,400 to 20,000, with polymorphonuclear neutrophils predominating. Four cultures were negative for Bacillus melitensis and for typhoid and paratyphoid bacilli. One culture showed Staphylococcus albus, which was considered a contamination. Hourly smears taken on one day (eleven in all) were negative for parasites of malaria and relapsing fever. Agglutinations for the organisms of typhoid, paratyphoid, malta fever and tularemia and for meningococci were negative; they were positive for typhus (Bacillus proteus X 19) in titers of from 1 : 10 to 1 : 80. The Wassermann reaction of the blood was negative. There was an indirect reaction to the van den Bergh test; the icteric index was 6 at one time and 7 at another.

Other Findings.—Flat roentgenograms of the sinuses, chest and abdomen were normal. A barium sulphate enema given on the twenty-first day showed the colon to be redundant throughout and the appendix to be normal in size and position.

At the end of the third week the patient began to show a slight icteric tinge in the sclerae and a pallid skin. Fulness and resistance in the right upper quadrant were also detected. This region soon gave signs of increased dulness, spasm and moderate tenderness. Graham-Cole tests were performed on the twenty-fourth and twenty-sixth days. Both were positive in that the gallbladder was not visualized.

Operation.—On September 12, the patient was operated on by Dr. Robert Linton. The preoperative diagnosis was cholecystitis and possible pyelophlebitis. The abdomen was opened by a right paramedian incision. A small amount of clear, straw-colored fluid was present. The liver extended about 3 cm. below the costal margin. The gallbladder was enlarged, distended and very tense. The appendix was in the right lower quadrant. Its tip showed evidence of old inflammation. There was no sign of a Meckel's diverticulum or of mesenteric adenopathy. Both kidneys were normal. The gastrohepatic ligament was very thick and indurated, and at the point where it joined the pancreas there was an inflammatory mass from 3 to 4 cm. in diameter. After appendectomy the gallbladder was aspirated; turbid bile was obtained. The wall was much thickened, especially the mucosa. A tube was inserted into the bladder, and a cigaret wick was placed alongside. Thus, surgical drainage of the biliary passage was the treatment chosen in preference to cholecystectomy. The latter procedure would have made proper drainage difficult because of the complicating relationship between the inflammatory mass in the gastrohepatic ligament and the common duct.

Pathologic Report on Appendix.—Gross examination gave negative findings. A small localized area in the mucosa showed a dense infiltration by polymorphonuclears. A diagnosis of acute appendicitis was made.

Bacteriologic Report on Culture of Bile.—Bacillus coli and B. proteus were found. A direct smear revealed streptococci. Though no growth occurred on blood agar plates inoculated directly, a scanty growth with hemolysis was obtained anaerobically.

Postoperative Course.—The day following operation the temperature returned to a normal level and remained there constantly. The amount of bile drained within twenty-four hours was from 5 to 10 ounces (141 to 283 cc.) at first; after ten days, it was from 2 to 3 ounces (56 to 85 cc.). On the eleventh day all the sutures

and the wick were removed; the wound was well healed. On the fourteenth day the tube fell out spontaneously. Two weeks later the defect in the wound was but 1 cm. in size, and the amount of bile on the dressing was negligible. The patient was discharged on the thirty-fourth day. During this period he had gradually recovered his appetite, and his weight had increased from 51 to 64 pounds (23.1 to 29 Kg.). When he was seen five months later in the outpatient department it was stated that he had gained 10 pounds (4.5 Kg.) more and remained free from symptoms, except for a certain nervousness. His appetite was fair.

During the next ten weeks the nervousness disappeared; the appetite became good; his weight rose to 78 pounds (35.4 Kg.) and he easily maintained an active school life. On May 17, 1933, eight months after the operation, another Graham-Cole test was performed. Again the gallbladder was not visualized.

OTHER CASES STUDIED

The table gives as much pertinent detail as could be gathered concerning the cases of cholecystitis in childhood in which there was no history of typhoid or any stones, as proved by operation or autopsy. The material from the literature was taken from the original articles. The 3 additional cases were found in the records of the Massachusetts General Hospital from 1870 to June, 1933. In the 710 cases of disease of the gallbladder of patients of all age groups who were operated on during that period, only these 3 fell into the special class under consideration.

Owing to the great variability of material and the lack of uniform considerations in the reports of the cases studied, there are many gaps in the information. This, plus the fact that the series of cases is small, necessarily means that in any analysis one may draw but limited conclusions. An endeavor was made to substantiate the observations and correlations, as far as possible, with figures.

Age.—Of the 27 patients 16 were between 8 and 14 years of age, and 11 were between about 3 and 6 years of age.

Duration of Illness Before Operation.—In 5 cases, or 18 per cent, the duration was a matter of hours; in 13 cases, or 50 per cent, it was between two and eight days; in 4 cases, or 15 per cent, about two weeks; in 1 case, five weeks, and in 2 cases, one year and two years respectively.

Associated Infections.—In 12 cases infection of the upper respiratory tract was a prominent feature in the past history (cases 3, 10, 14, 17, 18, 19, 20, 24, 27) or present illness (cases 3, 7, 12). On the other hand, in 14 cases there was a history of gastro-intestinal symptoms.

Appendix.—The relationship between the appendix and gallbladder in disease is of especial interest. In 17 cases the appendix was either normal or not mentioned; in the remaining 10 cases it was abnormal. In 2 of these (25 and 4) it had become perforated five and nine days, respectively, before the gallbladder apparently became involved.

Summary of Twenty-Seven Cases of Cholecystitis in Children with No History of Typhoid and No Stones

Case	Author	Date of Report	History	Duration of Illness Before Operation	Symptoms	Signs	Jaundice	(T) Temperature, F, and (P) Pulse Rate When First Seen	Blood Count When First Seen	Gallbladder	Appendix	Postoperative Course	Comment
1.	Riedel: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **14**: 8, 1905 Boy, aged 9 yrs.	1905	Always well	40 hrs.	Intermittent vomiting; pain in right upper quadrant; restless at night	Appeared very ill; resistant and very sensitive abdomen; gallbladder stood out under anesthesia	No	T, 100 P, 95	.....	Enlarged, distended, tense; red, except one green side; mucous membrane cyanotic; bile thick	Normal	Temperature normal within 6 days	Cholecystectomy; differential diagnosis, appendicitis; free fluid found in abdomen with fibrin coagulum
2.	Riedel: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **19**: 1, 1908 Girl, aged 13 yrs.	1908	Always healthy	12 days	Ill for 2 days at onset; 4 days before examination epigastric pain and vomiting; violent vomiting for 2 days	Appeared ill; pulse weak; no abdominal distention; no visible peristalsis	Yes	P, 70	.....	Size of hazelnut; no distention; edema at its neck and between it and liver; bile clear	Normal	Vomiting for a few days; jaundice persisted longer; within 6 months, well nourished	Cholecystectomy; differential diagnosis, high intestinal obstruction; no free fluid found; duodenum inflamed; swollen glands in hepatoduodenal ligament
3.	Montenbruck: Deutsche med. Wchnschr. **35**: 1065, 1909 Boy, aged 5 yrs.	1909	For 6 mos. upper respiratory and gastro-intestinal catarrh with fever	11 days	Ill 11 days with scarlet fever; 9 days before examination violent vomiting with extreme abdominal pain; fever	Very ill; groaning and crying; abdomen distended; tender right upper quadrant	No	T, 103.5	.....	Size of 3 fists; tense; 250 cc. of green stringy bile aspirated	.....	Afebrile; stool on fifth day; discharge on twenty-second day	Cholecystectomy; differential diagnosis, abscess of the liver; bile normal microscopically
4.	Wharton: Tr. Am. Surg. A. **27**: 540, 1909 Boy, aged 13 yrs.	1909	.....	3 days	Diffuse epigastric pain, referred to umbilicus; nausea and vomiting; 2 days later exacerbation and operation Pain in right upper quadrant on ninth day after appendectomy	Abdomen distended and diffusely tender; tender rectal mass in right iliac region Mass felt in right upper quadrant	No	T, 99.4	.....	Distended; 200 cc. of pus evacuated	Perforated; 20 cc. of pus in peritoneal cavity	Tube removed on tenth day; abscess drained on fourteenth day; later, pneumonia before discharge	Appendectomy; 22 days later, cholecystotomy with drainage
5.	Pybus: Lancet **1**: 1812, 1914 Boy, aged 6 yrs.	1914	.....	5 days	Onset: Bilious attack; for 3 days very ill but no pain; no constipation; recurrence 1 day before examination, with severe pain in right side of abdomen	Pale and sweating; tongue coated white; right upper quadrant distended, tender, spastic and revealing a mass	No	T, 101 P, 132	.....	Size of hen's egg; tense and inflamed; contained bile-stained pus	.....	Temperature normal on fourth day	Cholecystotomy; differential diagnosis, subhepatic appendicitis Bile culture: B. coli

6. Jacobson [18] Boy, aged 13 yrs.	1920	.....	6 days	Diffuse epigastric pain with occasional acute exacerbations	Moderately tender epigastrium	Yes	T, 100.6	8,000	"Subacute cholecystitis"	.....	.....	Cholecystectomy
7. Farr: Arch. Pediat. 39: 574, 1922 Boy, aged 8 yrs.	1922	Three years before, ill 1 week, with vomiting and abdominal pain	1 week	General malaise for 6 days, then sore throat and vomiting; no pain in abdomen; no bowel trouble	Looked ill, apathetic and sallow; tongue coated; throat red; abdomen distended; tenderness on right side, including lumbar region; no spasm, mass (?) in right upper quadrant	....	T, 103 P, 128	36,000 PMN* 87%	Very distended; deposit of fibrin outside; wall thick; mucosa edematous; clear mucoid contents	.....	.....	Partial cholecystectomy with drainage; liver near bladder found studded with abscesses Cultures: bile, sterile; blood and abscesses Staph. aureus
8. Farr: Arch. Pediat. 39: 574, 1922 Boy, aged 13 yrs.	1922	Four years before, first attack of vomiting, pain in abdomen and jaundice; recurrences every few months, then every few weeks; marked dyspepsia	.....	Onset with chills, pain in abdomen and vomiting	.....	Yes	T, 101	35,000 PMN 95%	Enlarged; clear mucoid contents with small white kernels	Large and congested	Temperature normal within 8 days	Operation not described
9. Farr: Arch. Pediat 39: 574, 1922 Boy, aged 12 yrs.	1922	Two months before examination severe pain in right upper quadrant during an entire night; no radiation	4 days	Epigastric pain; vomiting after every meal; marked constipation	Appeared acutely ill; tongue coated: tender right lower quadrant; mass in right upper quadrant	....	T, 100	15,000	Enlarged and tense; inflamed; wall thick	Congested	Temperature rose to 103 F.; bile drained within 15 days	Operation not described
10. Farr: Arch. Pediat. 39: 574, 1922 Boy, aged 8 yrs.	1922	Never strong; rheumatic heart disease 4 years before examination; tonsillectomy and adenoidectomy 2 years before examination	2 days	General pains; anorexia; fever; constipation	General abdominal tenderness on deep palpation; slight spasm of right rectus abdominis muscle; rectal region tender on right	. . .	T, 103.4 P, 108-120	28,000 PMN 83%	Large and tense; bile expressed with difficulty	Slight infiltration PMN	Temperature normal within 6 days	Appendectomy

* PMN indicates polymorphonuclears.

Summary of Twenty-Seven Cases of Cholecystitis in Children with No History of Typhoid and No Stones—Continued

Case	Author	Date of Report	History	Duration of Illness Before Operation	Symptoms	Signs	Jaundice	(T) Temperature, F, and (P) Pulse Rate When First Seen	Blood Count When First Seen	Gallbladder	Appendix	Postoperative Course	Comment
11.	Fischer: Jahrb. f. Kinderh. **104**: 350, 1924 Girl, aged 11 yrs.	1924	.....	3 days	Sudden onset, with abdominal colic and vomiting; became worse	Appeared ill; weak; sunken facies abdominalis; abdomen distended; right upper quadrant tender and very spastic	....	T, 100.5 P, 120	.....	Markedly distended; fibrin over fundus; wall thin and dull; bile turbid	Not remarkable	Temperature normal within 3 days; no more pain	Cholecystectomy and appendectomy Bile culture: Staph. aureus
12.	Fischer: Jahrb. f. Kinderh. **104**: 350, 1924 Girl, aged 2½ yrs.	1924	.....	8 days	Eight days before examination came down with scarlet fever; for 3 days had pain in the abdomen; vomited once	Appeared weak and pale; no rash; throat and tonsils red; large abscess on right arm, with large axillary gland; abdomen distended, especially on right; midepigastrium tender and spastic, with a palpable mass	No	T, 99.3 P, 120	.....	Size of a fist, cystlike; very distended; wall thin, bluish and transparent; bile thin and pure	.....	Distention of abdomen subsided; infection of right middle ear; bronchitis; diarrhea; died 15 days after operation	Cholecystotomy; autopsy showed common duct incompletely obstructed by glands at the duodenum, which were nonsuppurative and the size of hazelnuts and walnuts
13.	Hamerton: Brit. M. J. **1**: 778, 1925 Girl, aged 3 yrs.	1925	For 18 months vague abdominal pains, not severe; no jaundice	4 days	Four nights before examtion awakened by vomiting and severe abdominal pain; next day, no symptoms; during entire night before examination had abdominal pain and vomiting	Looked ill; exhausted; face flushed; abdomen distended and spastic (especially right upper quadrant) and tender (especially to right of umbilicus); rectal examination negative; under anesthesia a tense and mobile mass felt under right costal margin	No	T, 100 P, 128	.....	Distended to 5 by 1½ in.; shiny, mottled purplish; mucous membrane inflamed; 20 cc. of clear green fluid aspirated	.....	Uninterrupted	Cholecystotomy Cultures: bile, sterile; peritoneal fluid, Staph. albus and Staph. aureus

14. Snyder [1b] Boy, aged 5½ yrs.	1925	Long period of ill health with digestive upsets; had measles, pertussis, scarlet fever; fracture of leg 1 month before examination	1 day	Severe abdominal pain with nausea and vomiting 1 day before examination	Right side of abdomen rigid; McBurney's point painful	No	T, 102 P, 110	13,000 PMN 78%	Enlarged and tense; could not be emptied; thick bile and pus aspirated	Acutely inflamed	Good recovery	Cholecystotomy with drainage, and appendectomy Bile culture: mixed infection
15. Snyder [1b] Boy, aged 9½ yrs.	1925	Scarlet fever at 5 years of age	About 3 days	Severe abdominal pain, with nausea and vomiting; permission for operation refused for 2 days; symptoms aggravated	.....	....	.....	13,000 PMN 75%	Enlarged and distended; could not be emptied; purulent bile aspirated	Moderately inflamed	Good recovery	Cholecystotomy with drainage, and appendectomy Bile culture: mixed infection
16. Muller [6b] Boy, aged 4 yrs.	1926	.....	2 weeks	For 2 weeks intermittent abdominal pain on right; 2 days before examination terrific pain there, also in both knees and in right arm; repeated vomiting; constipation; on day before examination similar pain in abdomen and vomiting	Crying with distress; abdomen distended and spastic; tenderness, especially to right of umbilicus; under anesthesia an oblong tumor felt in right upper quadrant extending to below level of the umbilicus	....	.....	.....	Enormously distended; wall thin; grayish green; serosa and mucous membrane inflamed and infiltrated by white blood corpuscles; subserosa edematous; 50 cc. of clear yellow fluid emptied	Normal	Abdomen soft within 2 days; stool on third day; discharged on fourteenth day	Cholecystectomy; 200 cc. of fluid found in peritoneum Bile culture sterile
17. Stammler: Monatschr. f. Kinderh. 35: 481, 1927 Boy, aged 5 yrs.	1927	Susceptible to colds; 6 months before examination had rash; never any severe gastrointestinal upsets	3 days	Sudden onset of "stomachache"; became worse; anorexia and vomiting, then colicky pains with crying; constipation	Very ill, with pale sunken facies; rapid, superficial respiration; tongue dryly coated; abdomen distended and tender, especially in right upper quadrant where mass 6 cm. long was felt	No	P, 100	.....	Tensely distended; purplish; could not be emptied; wall inflamed; a spot of necrosis in the mucosa; purulent bile aspirated	.....	Drain out on sixth day; discharged within 1 month; well and free from symptoms 9 months later	Cholecystectomy; differential diagnoses, high appendicitis and intussusception; peritoneum about gallbladder found inflamed; glands mesial to cystic duct swollen Bile culture: sterile

Summary of Twenty-Seven Cases of Cholecystitis in Children with No History of Typhoid and No Stones—Continued

Case	Author	Date of Report	History	Duration of Illness Before Operation	Symptoms	Signs	Jaundice	(T) Temperature, F, and (P) Pulse Rate When First Seen	Blood Count When First Seen	Gallbladder	Appendix	Postoperative Course	Comment
18.	Potter [7] Girl, aged 4½ yrs.	1928	Influenza 2 years before examination	2 years	Stomach trouble for 2 years with three specific attacks of vomiting and fever; for 2 days pain in entire right side of abdomen	Abdomen distended and tender, especially to right of umbilicus; spasm of right rectus abdominis muscle	Yes	T, 103 P, 136	20,000 PMN 96%	Moderately enlarged; dark; could not be emptied; wall thick	Retrocecal, distention; gangrenous tip	Acetonuria for 11 days discharged on twentieth day; in good health 6 months later	Appendectomy; adhesions found between biliary tract and duodenum; when these were broken, bladder emptied easily
19.	Potter [7] Boy, aged 11 yrs.	1928	Influenza 1 year before examination	1 year	Dizzy spells for 1 year, with drowsiness and vomiting; has shown jaundice	Abdomen distended and tender on right side, especially at McBurney's point	Yes	T, 102.4 P, 106	23,000 PMN 94%	Enlarged; wall gray and edematous; 178 cc. of bile-streaked mucus aspirated	High-seated, inflamed	Mucus drained within 6 days, then bile; temperature normal within 10 days	Cholecystotomy with drainage Bile culture sterile
20.	Vollmer: Ztschr. f. Kinderh. **49**: 200, 1930 Boy, aged 6½ yrs.	1930	Pharyngitis, with no fever vomiting or anorexia 2 weeks before examination	31 hrs.	Eight hours before examination was struck forcefully in the abdomen by a football; well until eating, a few hours later; then abdominal pain and repeated vomiting; pain was localized in right upper quadrant and disappeared when spasm developed	Apathetic and drowsy; no abdominal distention; before spasm, a tender cylindric tumor was felt in right upper quadrant	Yes	T, 97	Many PMN	Size of a pear; tensely distended; wall inflamed; purulent fluid aspirated	Normal	Uneventful recovery	Cholecystotomy and appendectomy; differential diagnoses, atypical appendicitis and intussusception (barium enema suggested the latter, perhaps because gallbladder pressed on ascending colon)
21.	Montgomery [1a] Boy, aged 10 yrs.	1932	Always healthy; measles 2 years before examination	16 hrs.	Awakened by severe abdominal pain; vomited; pain most marked in epigastrium; nearly constant, sharp, cramplike	Abdomen tender and spastic on right, especially at level of and above umbilicus	No	T, 101.5 P, 100	14,000	Enlarged; firmer than usual; dark red; bile dark and thick	Normal	Uneventful recovery; discharged within 23 days	Cholecystostomy and appendectomy; differential diagnosis, acute appendicitis; adhesions between gallbladder and omentum Bile culture: B. coli

				constant, sharp, cramplike								Bile culture: B. coli
22. Montgomery [1a] Boy, aged 6 yrs.	1932	.....	16 hrs.	Sudden severe cramplike general abdominal pain, with vomiting; gradual localization to lateral edge of right rectus abdominis muscle	Painful expression; grunting respiration; abdomen rigid; local tenderness and spasm to right of and above umbilicus	No	T, 101	17,000	Red; wall thick and friable	Normal	Died within 48 hours, of general peritonitis	Cholecystectomy Bile culture: hemolytic streptococci
23. Bittner [6a] Girl, aged 5½ yrs.	1932	.....	.....	.....	Critical condition; appearance of fulminating peritonitis	....	.....	.....	"Acute gangrenous, ulcerative;" wall was crumbling distally and was perforated posteriorly	Normal	Died	Operation not described; diffuse peritonitis, with mucopurulent odorless yellow exudate Cultures negative for typhoid bacilli
24. Holbrook Girl, aged 10 yrs.	1934	Scarlet fever 6 months before examination	1 week	Sudden onset of abdominal cramps, nausea and vomiting; daily recurrence of cramps; vomited again on day before examination; had chill on day of examination, with vomiting and pain in right flank; constipated	Tongue coated white; tonsils enlarged; abdomen distended and firm; right upper quadrant more tender and rigid than left; edge of liver felt 2 in. (5.08 cm.) below ribs; small tender tumor felt to right of umbilicus	Slight	T, 100 P, 110	18,000	Enlarged and distended; could be emptied; mucosa normal; clear green fluid aspirated	Normal	Died on fourth day, of peritonitis	Cholecystectomy; considerable cloudy fluid found in abdomen; gallbladder adherent to much enlarged liver Cultures: abdominal fluid, sterile; bile, large micrococci
25. Holbrook Boy, aged 14 yrs.	1934	No previous attacks	10 days	Sudden onset of general abdominal pain 5 days before examination, which persisted intermittently; became worse on right; vomiting for 3 days before examination; appendectomy	Rather ill; thin and pale; tongue coated; abdomen distended, tender and spastic, especially on right; large mass in right lower quadrant	No	T, 99 P, 120	30,000	Distended tensely; wall had 3 small gangrenous areas; purulent bile evacuated	Inflamed, gangrenous, perforated; concretion present	Temperature from 100 to 102 F. following appendectomy; wicks and tube out on fifth day after cholecystostomy; septic temperature for 2 weeks; discharged on thirty-second day	Appendectomy and cholecystostomy; abscess in right lower quadrant; no direct connection between gallbladder and abscess Cultures: appendix, B. coli and streptococci; bile, sterile
				Symptoms not described 5 days after operation	Tender and rigid in right upper quadrant 5 days after operation		T, 102.4 P, 120					

Summary of Twenty-Seven Cases of Cholecystitis in Children with No History of Typhoid and No Stones—Continued

Case	Author	Date of Report	History	Duration of Illness Before Operation	Symptoms	Signs	Jaundice	(T) Temperature, F, and (P) Pulse Rate When First Seen	Blood Count When First Seen	Gallbladder	Appendix	Postoperative Course	Comment
26.	Holbrook Girl, aged 14 yrs.	1934	Negative for gastrointestinal symptoms	5 days	Five nights before examination, awakened by dull epigastric pain, which persisted intermittently and became worse; no radiation; 3 days before examination, vomited once; stools watery	Comfortable, rather drowsy; tongue coated; right upper quadrant tender and spastic; no masses felt	No	T, 101	20,300	Not enlarged, "thickened;" wall fibrotic; papillary hyperplasia of mucosa; general infiltration by wandering cells	Normal on gross examination; microscopy showed slight fibrosis	Temperature normal on fifth day; wick removed on eighth day; discharged on twelfth day	Appendectomy and cholecystectomy; gallbladder bound with fresh adhesions to transverse colon; many large firm glands in mesocolon
27.	Holbrook Boy, aged 11 yrs.	1934	Measles at 5 years; pertussis at 7 years; scarlet fever at 9 years	5 weeks	Onset of fatigue, fever and vomiting 2 weeks before examination, with quick remission; fever, chill and delirium 2 days later; 1 week before examination: temperature, 104 F., pain in right lower quadrant, anorexia; 4 days before examination: nose bleed and cough; 2 days before examination: temperature, 103 F., and vomiting For next 3 weeks ate poorly, lost weight and color; had chills and fever	Did not appear acutely ill; thin, pale, apathetic; skin dry, tongue coated, throat red Three weeks later, slight spasm and tenderness in right upper quadrant	Very slight	T, 103.2 P, 130	7,000 PMN 82%	Two Graham-Cole tests positive; enlarged and tense; distention; wall much thickened, especially the mucosa; turbid bile aspirated	Normal on gross examination; microscopy showed a patch of acute inflammation	Wick out on eleventh day; tube out on fourteenth day; bile drained for 1 month; discharged on thirty-fourth day; 8 months later Graham-Cole test positive and health excellent	Appendectomy and cholecystostomy; differential diagnosis, undulant or typhoid fever, later appendicitis and pyelophlebitis; a small amount of clear fluid found in abdomen; liver, 3 cm. below rib; gastrohepatic ligament indurated, with inflammatory mass next to pancreas Bile culture: B. coli, B. proteus, anaerobic streptococci

Appendicitis was a complication in at least 5 cases and probably in more. Yet the symptomatology in these cases was remarkably like that in all the others.

Symptoms.—Ninety per cent of the patients, both those with normal appendixes and those with abnormal appendixes, vomited; 90 per cent also had pain. In the group of those with normal appendixes the pain tended to localize in the right upper quadrant; in the group with abnormal appendixes, about the umbilicus or right lower quadrant. Thirty-three per cent of the patients in both groups were constipated, and 33 per cent had intermittent attacks of the symptoms of their illness. Of the 27, 22 had abdominal pains which characteristically were sudden, severe and colicky and which were accompanied by vomiting. They commonly occurred in attacks, which, if mild at first, became progressively worse. Fever or chills occurred only six times.

Signs.—In 19 cases there were signs in the right upper quadrant. Palpable masses were found in 11, tenderness and spasm in 8. Sixteen of the patients appeared acutely ill, drowsiness, distress, pallor, sunken facies, weak pulse, quickened respirations and sweating, constituting the major signs. Abdominal distention occurred in 12 cases, jaundice in 8 and coated tongue also in 8.

Operative Findings in the Gallbladder.—The gallbladder was markedly enlarged, distended and tense in 22 cases. The bile was purulent or thick in 12, clear and thin in 5 and mucoid or stringy in 4. Surrounding adhesions, edema or inflammation were found in 7 cases, and the gallbladder could not be emptied in 5 cases.

Cultures of Bile.—Fifteen cultures were made. Seven proved to be sterile. The positive growths included Staphylococcus aureus, large micrococci, hemolytic streptococci, anaerobic streptococci, B. coli (three times) and "mixed infection" (two times).

Preoperative Differential Diagnosis in Cases Without Appendicitis.—In 6 cases the diagnosis was appendicitis; in 2, intussusception; in 1, intestinal obstruction, and in 1, abscess of the liver.

As the report of my case indicates, a disease to be considered in the differential diagnosis of febrile cholecystitis is undulant fever. Recently, Fairweather [9] reported a case of undulant fever which simulated subacute cholecystitis to a marked degree, with a swinging temperature, vomiting and anorexia and tenderness in the right upper quadrant. He believed that mild inflammation of the gallbladder was probably present. On the other hand, Simpson and Bowers [10] reported negative findings in pathologic studies of gallbladders removed from 2 patients with undulant fever as a result of an incorrect diagnosis of cholecystitis.

9. Fairweather, D. S.: Lancet **1**:613 (March 19) 1932.
10. Simpson, W. M., and Bowers, L. G.: Am. J. Surg. **7**:597, 1929.

COMMENT

It is evident that the case reported is unusual. There was pain on only one occasion; the patient vomited but twice, and for the three weeks during which he was under observation a striking dissociation existed between the findings listed on the chart and the physical signs. Babcock [11] wrote that long continued fever, without other symptoms, may result from infection of the gallbladder. In such cases the bile may be free from pus. With cholecystectomy a cure is effected. Perhaps low grade infection with minimal inflammation is the explanation of latent cholecystitis. Indeed, Behrend [12] remarked that a gallbladder may be distended to the bursting point and still be painless, presumably because "signs of inflammation are absent." The category into which my case fits best was described by Jacobson [13] as an atypical biliary group of cases without colic, presenting a rather dull ache in the right upper quadrant with tenderness, nausea and vomiting, with or without jaundice, and, especially, displaying septic fever and leukocytosis. I believe that the abnormalities of my patient's temperature must have been due partly to associated cholangeitis, because of the marked subsidence following simple drainage of bile, without removal of the bladder.

Thus, any unexplained fever and many acute and chronic abdominal conditions in children should call for examination of the gallbladder. The main difficulty in the diagnosis of cholecystitis in children is the failure to suspect it.[8] After the diagnosis has been made the consideration arises that, as in adults, there is not infrequently associated appendicitis.[14] This may or may not complicate the clinical picture. In any operation for cholecystitis, except in cases with fulminating infection, the appendix should be inspected as a routine.

SUMMARY

1. An unsual case of cholecystitis is reported in a boy, aged 11, who for five weeks had an unexplained septic fever and in whom signs in the right upper quadrant finally developed. He had never had typhoid fever. Two Graham-Cole tests were positive. Cholecystostomy with biliary drainage was followed by a dramatic return of the temperature to normal.

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11. Babcock, W. W.: Cholecystectomy and Cholecystic Toxemia, J. A. M. A. **65**:1428 (Oct. 23) 1915.

12. Behrend, M.: Surgical Diseases of the Gallbladder, Liver and Pancreas, Philadelphia, F. A. Davis Company, 1927.

13. Jacobson, C.: Gallbladder Disease; A Statistical Study, Arch. Surg. **1**:310 (Sept.) 1920.

14. Rivers, A. B., and Hartman, H. R.: Abdominal Exploration in Cases Diagnosed Cholecystitis and Cholelithiasis Before Operation, Arch. Int. Med. **45**:523 (April) 1930.

The hectic fever is attributed partly to associated cholangeitis.

Eight months later the boy's health was excellent. However, he still showed a positive reaction to the Graham-Cole test.

2. Twenty-six comparable cases are presented in tabulated form, with as much essential detail as was available. Three were found in the records of the Massachusetts General Hospital; the rest are from the literature. All the patients were under 15 years of age and had non-typhoid cholecystitis without stones.

3. Comparison of the various clinical aspects of these selected cases shows principally that: (*a*) in 50 per cent the illness was of from two to eight days' duration; (*b*) in nearly 50 per cent infection of the upper respiratory tract was a prominent feature in the history; (*c*) the majority of patients had symptoms of sudden, colicky abdominal pain, with vomiting, appeared acutely ill and showed signs in the right upper quadrant; fever was uncommon; (*d*) in 37 per cent there was associated appendicitis of varying degree.

Pediatric Biographies

THOMAS FULLER

1654-1734

A NOTE ON THE HISTORY OF CHICKENPOX

JOHN RUHRÄH, M.D.
BALTIMORE

Thomas Fuller was born at a country house in the parish of Brightling, Sussex, on June 24, 1654. He was educated at Queen's College, Cambridge. He received the degree of bachelor of medicine in 1676 and of doctor of medicine in 1681, and was admitted an extralicentiate of the College of Physicians in London in 1679. He settled in Sevenoaks, in Kent, where he was a much beloved practitioner for the remainder of his life.

He was an ardent champion of the poor, and when quite old he compelled the managers of a charity fund of the town to produce their accounts in Chancery and in the future to be subject to annual election.

He wrote a number of medical works: "Pharmacopoeia extemporanea," 1702; "Pharmacopoeia bateana," 1718; "Pharmacopoeia domestica," 1723, and "Exanthematologia: Or an Attempt to Give an Account of Eruptive Fevers, Especially of the Measles and Smallpox," 1730. Among his lay books are found "Introductio ad prudentiam: Or Directions, Counsels, and Cautions Tending to Prudent Management of Affairs in Common Life," 1727, compiled for the use of his son, John Fuller; "Introductio ad prudentiam: Or the Art of Right Thinking, Assisted and Improved by Such Notions as Men of Sense and Experience Have Left Us of Their Writings, in Order to Eradicate Error and plant Knowledge," 1731, and adages, proverbs, wise sentiments and witty sayings, ancient and modern, foreign and British.

In 1703 he married Mrs. Mary Plummer. He wrote the following tetrastric for himself:

> Ante obitum felix cantabo epicedia nostra;
> Octoginta annos sum passus tristia terrae,
> Mors dabit his finem: mecum laetamine amici,
> Aeternum post hac caelorum laeta tenebo.

Happy before my death I will sing my funeral song. For eighty years I have borne the sorrows of the earth. Death will make an end of them. Rejoice with me my friends, for henceforth I shall forever have the joys of heaven.

RITTELEN OR CHICKEN-POX

THEY are small red Pustulary Eruptions, about the Bigness of Mustard-Seed, more or less numerous, invading with Fever and Cough, and sometimes sore Throat; now and then with Bleeding at Nose, Vomiting, and other usual Signs of the Small-Pox or Measles; but this Distemper is less dangerous than either of them; they vanish away like the Measles, and have been in some Years noted to go off with a Diarrhea.

SOMETIMES they come alone; sometimes have been seen sprinkled in among the Measles; all which shews them to be a particular Kind distinct from the Measles.

EXANTHEMATOLOGIA:

Or, An ATTEMPT to Give a

Rational ACCOUNT

OF

Eruptive FEVERS,

ESPECIALLY OF THE

***Measles* and *Small Pox*.**

In TWO PARTS.

PART I. Of the Blood, the Air, Venoms, Infection; Fevers of all Kinds in general, and of such in particular as are Morbillous with Spots, or Variolous with Pustles; and in Specie, of most of the spurious Sorts mentioned in Books, and met with in Practice; with their Varieties, Descriptions, Names, &c. but more professedly and fully of the True MEASLES.

To which is prefix'd,

A Delineation and Comparison of the OLD and NEW PHILOSOPHY.

In a *Dialogue*. By an unknown Hand.

PART II. Of the SMALL-POX, its Nature, Genius, and Production; of its Causes, Differences, Diagnostic and Prognostic Signs; also of Prevention, Management, Medicines, and Methods to be observed and used in the Cure of the *same*; and its Symptoms, from its first Invasion, through all its Periods and Progress, to its Conclusion: And lastly, of the BLEEDING POX.

To which is added,

***An* APPENDIX *concerning* INOCULATION.**

The whole Illustrated with many New, Curious, and Useful Particulars.

By THOMAS FULLER, *M.D.*

LONDON:

Printed for CHARLES RIVINGTON, and STEPHEN AUSTEN, in St. *Paul's* Church-yard.

M.DCC.XXX.

Title page of Fuller's book on infectious diseases.

I have adventur'd to think this is that which among our Women goeth by the Name of Chicken-Pox, and might be so called from the Smallness of the Specks, which they might fancy looked as tho' a Child had been picked with the Bills of Chickens.

BUT it is said, that Poultry and Turkeys are subject to a Disease coming out with red Pimples, tho' not many, that soon dry up into Scabs, but are not apt to leave Scars or Marks.

THIS Chicken-Pox, and several others of the little spurious Sorts, are Distempers that have all of them a distinct material Cause, and therefore differ not only in Degree, but in Essence also from one another.

This material Cause is not much entangled, and detained in the Size of the Blood; but being of a sharper Nature than that of the Crystals, acts, tho' not so fiercely on the Globules as to put them into a febrile Ebullition, yet so as to break them a little, and cause them to shed off some of their loosest Particles, with which being join'd, they come out in red Pimples, without the Help of a considerable Fever, or the Concurrence of remarkable Symptoms.

FROM FLEA-BITES

THESE are Spots perfectly round and flat, without the least Protuberance, or Roughness, and are much larger than either the Measles or Small-Pox are at first coming out.

IF they be fresh, they shew Marks of the Bite, which is a little red Centre, visibly distinct from the rest of the Spot; and that Centre will not disappear, tho' it be so pressed with the Finger as to force away the Blood from it, and make it look whitish about it.

IF they are not newly made, they are not of so fair a Damask Red as the Measles and Small-Pox are, but look more dead and dusky.

THEY never grow at all, nor keep coming out from Day to Day, but are all chancing.

IT is said they may be obliterated, if Bean Meal, wet into a Paste with Vinegar, be laid to them.

THEY come without any Indisposition, Signs, or Symptoms, that are usual before the Small-Pox or Measles.

OF A NURSE

Though it is impossible to meet with a Nurse every day so Qualify'd for the Business, as to have no Faults or Failings, yet the more she cometh up to the following Particulars, the more she is to be liked. It is therefore desirable that she be,

1. Of a middle Age, fit and able to go through with the necessary Fatigue of her Undertaking.

2. Healthy, especially free from Vapours, and Cough.

3. A good Watcher, that can hold sitting up the whole Course of the Sickness.

4. Quick of Hearing, and always ready at the first Call.

5. Quiet and still, so as to talk low, and but little, and tread softly.

6. Of good Sight, to observe the Pocks, their Colour, Manner, and Growth, and all Alterations that may happen.

7. Handy to do every Thing the best way, without Blundering and Noise.

8. Nimble and Quick a going, coming and doing every Thing.

9. Cleanly, to make all she dresseth acceptable.

10. Well-Tempered, to humour, and please the Sick as much as she can.

11. Chearful and Pleasant; to make the best of every Thing, without being at any time Cross, Melancholy, or Timorous.

12. Constantly careful, and diligent by Night and by Day.

13. Sober and Temperate; not given to Gluttony, Drinking or Smoaking.

14. Observant to follow the Physician's Orders duly; and not be so conceited of her own Skill, as to give her own Medicines privately.

15. To have no Children, or others to come much after her.

Thomas Fuller died on Sept. 17, 1734. Three years before, during an illness, his death was prematurely announced in the *Gentleman's Magazine*. He was buried in Sevenoaks Church. There is a portrait by J. Tymewell, engraved by G. Vertue, in the "Pharmacopoeia domestica."

Fuller was the first English writer to point out how to distinguish between flea bites and the eruption of infectious diseases, and was the first Englishman to set down the qualifications necessary in a nurse for the sick. His principal medical work, "Exanthematologia," was published in London in 1730 by Charles Rivington and Stephen Austen. It contains interesting material on what was thought about the infectious diseases in those days and one of the best of the early accounts of chickenpox, perhaps the earliest in the English language.

News and Comment

UNIVERSITY NEWS

Privatdozent Dr. Otto Ulrich of the University of Munich has been made director of the Kaiserin Auguste-Victoria-Haus in Charlottenburg with the title of Extraordinary (Associate) Professor.

Dr. Albrecht Peiper of the University of Berlin has been made director of the Pediatric Clinic at the University of Bonn.

Dr. Völkers has been appointed chief physician in the Children's Hospital in Gelsenkirchen.

Dr. Boucomont has been made chief of the pediatric clinic, and Dr. Cabanac head of the orthopedic clinic, in the faculty of medicine of Montpellier.

Dr. G. Salvioli has been given the chair of pediatrics at the University of Siena.

Dr. L. Auricchio has accepted the chair of pediatrics at the University of Sassari.

Dr. G. Mouriquand, chief of the pediatric clinic of the University of Lyon, has been named the corresponding member of medicine, Academy of Medicine of France.

GENERAL

Postgraduate Courses in Pediatrics.—The usual courses for practitioners will be held in Vienna from May 28 to June 10. These will include courses in pediatrics as well as other branches.

SOCIETY NEWS

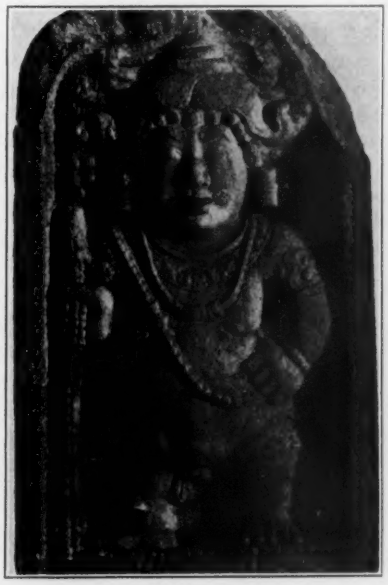
American Association on Mental Deficiency.—The annual meeting of the American Association on Mental Deficiency will be held at the Hotel Waldorf Astoria, New York, May 26 to 29, 1934. The Saturday session, May 26, will be given over to the sociologic, phychologic and special educational aspects of the problem in order that local social workers and school teachers may have an opportunity to attend without interfering with their regular duties. The Tuesday afternoon session will be a conjoint meeting with the American Psychiatric Association. Data as to the program may be obtained from the secretary, Dr. Groves B. Smith, Godfrey, Ill.

Pediatrics in Art

ACHONDROPLASIA

JOHN RUHRÄH, M.D.
BALTIMORE

In the museum at Colombo there is a bas-relief which was taken from the ramp of a stairway in one of the temples of Amurâdhapura, in the island of Ceylon. The work dates from the eighth century and is evidently a portrait of one of the guardians of the temple who was named Dwârpâla. The representation shows the normal sized head



Bas-relief in one of the temples of Amurâdhapura in Ceylon.

with the short body and very short arms and legs and the well developed genitalia. The curved little finger is wanting in this portrayal.

Achondroplasic dwarfs were popular subjects with ancient artists as well as with the more modern ones, and a fair-sized book could be made of these reproductions alone. One of the most ancient representations is that of the dwarf Khnoumhotpou, who had a large tomb at Sakkarah and whose statue now stands in the museum at Boulaq. Some of these dwarfs were deified as Bes, who is usually represented in panther skins and a feather crown. He looked after art, singing, dancing, children's games and childbirth. Ptah, another achondroplasic god of Egypt, was a self-created creator. Small varnished figures of these gods are often used as amulets.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

ACTION OF NORMAL SKIN ON BACTERIA. JUSTINE H. HILL and EDWIN C. WHITE, Arch. Surg. **26**:901 (May) 1933.

The object of the study reported in this paper was to evaluate by a new method the action of normal human skin on bacteria. The method employed was to apply skin to agar plate cultures of bacteria rather than to apply the bacteria to the skin. It was found that the skin inhibited the growth of bacteria in 13.7 per cent of the 1,444 tests. The skin varied greatly in its action on different types of bacteria. Its action was most marked on the gram-positive, spore-forming bacilli; it was less marked on the staphylococci and the gram-negative bacilli tested.

KAISER, Rochester, N. Y.

EXPERIMENTAL PRODUCTION OF MOTTLED ENAMEL. MARGARET C. SMITH and EDITH M. LANTZ, Arizona Agric. Exper. Stat. Tech. Bull., no. 45, 1933, p. 327.

Mottled enamel was produced experimentally by feeding fluorides or water containing fluorine to albino rats, dogs and guinea-pigs. The teeth of guinea-pigs are more resistant to changes caused by fluorine than are the teeth of human beings, rats or dogs. The percentage of fluorine in the rations which produced mottled enamel was as low as 0.0116. Mottled enamel was also produced by the subcutaneous and intramuscular injection of fluorine. If the mottling and corrosion have not proceeded too far, elimination of fluorine from the diet causes the teeth to regain their normal luster and appearance.

KUGELMASS, New York.

EFFECT OF VITAMIN A-FREE DIET ON RESISTANCE TO INFECTION BY SALMONELLA ENTERITIDIS. LELAND S. MCCLUNG and J. C. WINTERS, J. Infect. Dis. **51**:469 (Nov.-Dec.) 1932.

A marked increase in susceptibility to infections with Salmonella enteritidis injected intraperitoneally was shown in a group of animals fed a vitamin A-free diet for a period of seven weeks as compared with a control group which was similarly infected.

TOOMEY, Cleveland.

EFFECT OF DIETARY DEFICIENCY OF VITAMIN D IN RELATION TO INFECTION BY SALMONELLA ENTERITIDIS. LELAND S. MCCLUNG and J. C. WINTERS, J. Infect. Dis. **51**:475 (Nov.-Dec.) 1932.

The authors demonstrated that the lack of vitamin D causes only a slight increase in susceptibility to infection by Salmonella enteritidis and that the increase is certainly not as great as when vitamin A is absent in the diet.

TOOMEY, Cleveland.

BEHAVIOR OF BACTERIOPHAGE IN BODY FLUIDS AND IN EXUDATES. M. G. COLVIN, J. Infect. Dis. **51**:527 (Nov.-Dec.) 1932.

The experiments performed show definitely that the process of bacteriophagy in the body is markedly modified and that it is in no way as efficient as the bacteriophagy which occurs in the test tube. Blood serum seems to decrease the specific staphylococcic and streptococcic bacteriophagic lytic power.

TOOMEY, Cleveland.

RELATION OF GASTRO-INTESTINAL POISON TO OTHER TOXIC SUBSTANCES PRODUCED BY STAPHYLOCOCCI. ORAM C. WOOLPERT and G. M. DACK, J. Infect. Dis. **52**:6 (Jan.-Feb.) 1933.

These authors were able to produce a powerful staphylococcus gastro-intestinal toxin quite distinct from the hemolytic, dermotoxic and lethal toxins also found in all such preparations. Active immunization protected rhesus monkeys, but passive immunization failed.

TOOMEY, Cleveland.

ATTEMPT TO CONFIRM EXISTENCE OF A FILTRABLE CYCLE OF BACTERIA BY USE OF "K" MEDIUM. C. V. SEASTONE and MARY B. LAWRENCE, J. Infect. Dis. **52**:20 (Jan.-Feb.) 1933.

These experimenters could not repeat the work of Kendall and think that the work with the "K" (Kendall) medium as described is unsatisfactory. They suggest as a possible explanation for Kendall's success Bronfenbrenner's opinion that the "K" medium renders the filter more permeable, that the turbidity in the "K" medium is the result of a naturally developing precipitate in a medium in which changes occur easily and that the prompt appearance of growth on transplantation to broth is due merely to the fact that a few organisms are again transferred to a suitable medium. They do not believe that Kendall's experiments as described form "the slightest basis for the far-reaching conclusions drawn by him."

TOOMEY, Cleveland.

A METHOD FOR SECURING CLEAR SERUMS FROM THE MILK OF COWS AND GOATS FOR AGGLUTINATION TESTS, WITH SPECIAL REFERENCE TO UNDULANT FEVER. IVAN C. HALL and ROBERT LEARMONTH, J. Infect. Dis. **52**:27 (Jan.-Feb.) 1933.

In order to secure clear specimens of milk whey for purposes of agglutination, the authors recommend that the milk be treated with chloroform or carbon tetrachloride and rennet solutions. The specimens may be kept indefinitely without bacterial growth.

TOOMEY, Cleveland.

PRECISION PHOTOMICROGRAPHY IN BACTERIOLOGY. RALPH R. MELLON, J. Infect. Dis. **52**:60 (Jan.-Feb.) 1933.

The author gives a comprehensive review of the photography of bacteria. It contains details as to light, exposure, length and type of lens and other factors.

TOOMEY, Cleveland.

ANTIBODIES IN PLACENTAL EXTRACTS. CHARLES F. MCKHANN and FU TANG CHU, J. Infect. Dis. **52**:268 (March-April) 1933.

Protein material obtained from human placentas was found to be able to neutralize diphtheria toxin, blanch scarlet fever rashes, neutralize the poliomyelitis virus and prevent measles in exposed susceptible patients.

TOOMEY, Cleveland.

PHENYL-MERCURIC COMPOUNDS: THEIR ACTION ON ANIMALS AND THEIR PRESERVATIVE VALUES. L. A. WEED and E. E. ECKER, J. Infect. Dis. **52**:354 (May-June) 1933.

Weed and Ecker add further evidence to that previously printed that phenyl-mercuric-chloride is a safe bactericide when given orally, intraperitoneally or subcutaneously. The drug does not harm the bladder, does not inhibit or destroy the action of trypsin or pepsin, does not decrease agglutinins or precipitinogens, does not destroy toxins or venoms and does not inhibit the lytic action of lysozyme.

TOOMEY, Cleveland.

BODY BUILD AND ITS RELATION TO GASTRIC POSITION, FORM, SECRETION AND MOTILITY AND TO GASTROINTESTINAL EMPTYING RATE. WALTER J. SIEMSEN and ALFRED C. LEDOUX, J. Pediat. **2**:657 (June) 1933.

Comparative studies regarding gastric position, form, secretion and motility and the emptying time of the gastro-intestinal tract were carried out on twelve children of various body types. No definite relation was found between the secretory function, form and position of the stomach and body build. The literature on the subject is discussed.

LEMASTER, Evanston, Ill.

THE DISAPPEARING TIME OF DYES INJECTED INTRADERMALLY. SAMUEL AMBERG and ROLAND NUTTING, J. Pediat. **3**:31 (July) 1933.

Several different dyes were injected intradermally into normal persons, and the time of disappearance was measured. Such factors as the direction of migration of the dye in the electric field, the distinction between acid and basic dyes and the degree of aspersion could not be correlated with the length of time required for disappearance. Congo red and methylthionine chloride, U. S. P. (methylene blue) disappeared more rapidly when dissolved in serum than in salt solution. The results of experimental work of other workers in this field are cited.

LEMASTER, Evanston, Ill.

RENAL CHANGES IN THE RABBIT RESULTING FROM INTRAVENOUS INJECTION OF HYPERTONIC SOLUTION OF SUCROSE. HENRY F. HELMHOLZ, J. Pediat. **3**:144 (July) 1933.

Rabbits were given injections of a hypertonic solution of sucrose intravenously, and the resulting histologic changes in the kidneys and in the renal function were noted. Within an hour after one injection of sucrose the cells of the convoluted tubules were swollen. The enlargement of the cells persisted for about a week and normal size was regained within fifteen days. When the injections were repeated every three days there was a decided decrease in renal function, as measured by the output of phenolphthalein, but the renal function returned to normal two weeks after the last injection. There was no evidence of harm when the injections were given at intervals of from five to seven days.

LEMASTER, Evanston, Ill.

FUNCTION OF THE ADRENAL CORTICAL HORMONE AND THE CAUSE OF DEATH FROM ADRENAL INSUFFICIENCY. W. W. SWINGLE, J. J. PFIFFNER, H. M. VARS, P. A. BOTT and W. M. PARKINS, Science **77**:58 (Jan. 13) 1933.

Bilaterally suprarenalectomized dogs were kept healthy for months by daily injections of suprarenal cortical hormone. The function of the hormone is the maintenance of a normal volume of fluid in the vascular system. In the absence of the hormone, fluid is lost from the blood and passes into the tissues, the blood becomes more concentrated and viscous, the pressure falls and death occurs within from eight to twelve days. Blood urea and nonprotein nitrogen increase because of the decreased filtration pressure, and the flow of blood to the kidneys and the volume of urine decrease. Dogs still live after a loss of from 40 to 50 per cent of the plasma, and administration of the hormone restores them to normal. A 75 per cent loss of plasma is fatal. Hemorrhage is not compensated without the hormone. The hormone has no direct effect on blood pressure. Symptoms of suprarenal insufficiency and traumatic or secondary shock are perhaps both due to decreased blood volume; if so, the hormone should be beneficial in the treatment of cases of shock in man.

KUGELMASS, New York.

THE PRESENT POSITION OF SEROLOGY IN RELATION TO THE PATHOGENIC COCCI. H. J. PARISH, Brit. M. J. **2**:277 (Aug. 12) 1933.

It will be seen from this brief review of the serology of the pathogenic cocci that considerable advances have been made of recent years in connection with the

gram-positive group. As regards the meningococcus and gonococcus, the present position is much less satisfactory, but there are already some indications that more efficient antimeningococcic serums may become available. So far the serologist's most valuable contribution to the problem of the gonococcus has been the complement-fixation test.

AUTHOR'S SUMMARY.

THE ERYTHROCYTE SEDIMENTATION TEST: A CLINICAL AND EXPERIMENTAL STUDY. A. C. REES WALTON, Quart. J. Med. **2**:79 (Jan.) 1933.

This paper is an excellent review of the literature concerning the sedimentation rate of red blood cells in clinical medicine. The author's chief contribution to the knowledge of this phenomenon is the recognition of the relationship of the concentration of cells to the rate of sedimentation. He presents his own method of performing the test in a clear and concise manner and discusses the significance of a retarded or accelerated rate in various clinical conditions. He also points out the fact that proper interpretation of the test is necessary if the test is to be of benefit to the clinician. The report is rich in suggestions concerning new aspects of the test which lend themselves to investigation.

BRADFORD, Rochester, N. Y.

INTOXICATION EXPERIMENTS ON YOUNG RATS. YOSHIRO YAMAOKA, Monatschr. f. Kinderh. **58**:35 (May) 1933.

No one has been able to produce the syndrome of alimentary intoxication in rats. The authors tried all sorts of means such as large amounts of lactose and many types of purgative. Eventually they learned that in rats the best means of dehydration is to give a diet high in protein for from two to three weeks followed by a sudden withdrawal of water. This procedure causes a drop in weight of from 25 to 35 per cent, but no other toxic symptoms. Injection of coli toxin into a rat dehydrated in this manner did not produce the symptoms of alimentary intoxication.

GERSTLEY, Chicago.

BACTERIOPHAGE OF COLON AND PARACOLON BACILLI IN THE STOOL. EUGEN DEAK, Monatschr. f. Kinderh. **58**:143, 1933.

In fifty-one examinations of filtrates of the stools from twenty-five well children and twenty-six with diarrhea, as well as of the jejunal contents of seven dead children, no bacteriophage was found against colon or paracolon bacilli.

GERSTLEY, Chicago.

THE MICROTECHNICAL DEMONSTRATION OF INSOLUBLE CALCIUM SALTS IN THE TISSUES. G. GÖMÖRI, Virchows Arch. f. path. Anat. **286**:682, 1932.

The method described in this paper permits the staining of hard tissues such as bone, sclerotic tissue and other calcified tissues without previous decalcification. Small blocks of a maximum thickness of from 1 to 2 mm. are fixed in alcohol (a solution of from 80 to 96 per cent) for from two to three days. After washing in distilled water, the blocks are kept in a 1.5 per cent solution of silver nitrate without exposure to light for from six to ten days at room temperature. The silver nitrate solution is changed several times. The tissue is washed in distilled water for from three to four days in a dark room until the water gives only a slight opalescence with hydrochloric acid. The silver nitrate is reduced with a fresh solution of 5 per cent hypophosphite (crystals of sodium hypophosphorosum), which is slightly alkalinized by the addition of a few drops of tenth-normal sodium hydroxide. The reduction of the silver nitrate requires from four to six days, depending on the thickness of the blocks. They are washed again for from three to four hours, and the silver is fixed in a 4 to 5 per cent solution of sodium thiosulphate, which is changed several times. From this point on the blocks

may be exposed to light. They are washed again for at least twenty-four hours and decalcified with a 6 to 8 per cent solution of sulphosalicylic acid for from one to three days, the solution being replaced once or twice. The blocks are then washed once more and may be embedded, cut and stained in the usual way. The calcium appears as a deep black stain. Sections can be kept for a long time, even when exposed to the sun. The value of a method of this type for studies of the bone in rickets and other diseases of the bones is obvious.

SCHOENTHAL, New York.

TETANIGENIC SUBSTANCES IN THE THYMUS AND THE URINE: II. OCCURRENCE OF TETANIGENIC SUBSTANCES IN THE URINE OF CHILDREN AND ADULTS. H. SELZER, Ztschr. f. Kinderh. **54**:421, 1933.

Some time ago Nitschke suggested that spasmophilia is due to hyperfunction of the lymphatic system, and he claimed to have produced tetany in rabbits by the injection of extracts of the thymus or of urine from patients with spasmophilia. His results were, however, not entirely substantiated by other investigators, and hence there is no real proof that a calcium substance exists in the thymus or in the urine of spasmophilic children. The author adds further proof that the tetanigenic substance in the urine is not specific for spasmophilia. This is proved by the fact that only two of five specimens of urine from patients with tetany were tetanigenic, and that the urine from two nontetanic patients also caused convulsions in rabbits. The tetanigenic substances apparently occurred in the urines from children and adults in whom cell destruction was a prominent feature.

SHELLING, Baltimore.

EFFECT OF THYMUS MEDICATION ON THE FORMATION OF CALLUS. J. GYURIK and A. DAX, Orvosi hetil. **76**:626 (July 16) 1932.

Experiments were carried out on white mice 6 months of age. Artificial fractures were produced under sterile conditions. Thymus gland of calves was given in the form of an emulsion. The emulsion was prepared in 10 per cent physiologic solution of sodium chloride. One cubic centimeter of this was injected daily. The formation of callus was studied histologically and also roentgenologically. Both methods of control showed conclusively that the formation of callus is stimulated and hastened after the administration of thymus gland.

ZENTAY, St. Louis.

COLLOIDAL OSMOTIC PRESSURE (ONCOTIC PRESSURE) OF THE BLOOD IN EARLY LIFE. E. KYLIN, Acta pædiat. **14**:160 (Nov. 30) 1932.

The method of Krogh and Nakazawa was used to measure the oncotic pressure of the plasma, and the Pulfrich refractometer was used for plasma proteins. Thirty-nine patients ranging in age from new-born to 7 years were studied. During the first two months of life the oncotic pressure varies from from 200 to 270 mm. of water; the values rise with increasing age, rapidly at first and later more gradually, attaining the normal range of from 300 to 375 mm. (average, 340 mm.) about the end of the second year. The rise in total plasma proteins is approximately parallel. Throughout infancy and childhood the number of millimeters of water of oncotic pressure per gram of plasma protein varies between 30 and 46; for adults the normal range of the quotient is from 35 to 51.

MCINTOSH, New York.

Nutrition

AN EXPERIMENTAL STUDY OF "THE CONSTITUTIONAL FACTOR" IN THE ETIOLOGY OF RICKETS. ALFRED F. HESS and S. N. BLACKBERG, Am. J. Physiol. **102**:8 (Oct.) 1932.

A litter of four mongrel puppies was fed the Mellanby rickets-producing diet from the time of weaning. Two of the puppies were predominantly of one type,

a short-haired breed, whereas the other two were of a long-haired terrier type. One of the short-haired type was fed viosterol in addition and served as a control. Rickets developed in the remaining three dogs, and the degree of rickets varied directly with the predominance of the long-haired characteristic. The difference in the degree of rickets was marked, and the experiment demonstrated a definite constitutional tendency to rickets apart from diet and growth.

NOURSE, Cleveland.

EFFECT OF MUSCULAR WORK AND COMPETITION ON GASTRIC ACIDITY. FRANCES A. HELLEBRANDT and MERYE M. MILES, Am. J. Physiol. **102**:258 (Oct.) 1933.

Gentle exercise before or after a test meal augments gastric acidity. Protracted exercise is not necessarily depressing, but exhaustive muscular exertion, whether it precedes or follows a test meal, is associated with a diminution of the acidity of the gastric secretion to a level below the normal level during rest, and the decrease is greatest when the exercise is accompanied by emotional excitement.

NOURSE, Cleveland.

THE EFFECT OF BANANA POWDER FEEDING ON THE FECAL FLORA OF INFANTS. BERNARD S. KAHN, Arch. Pediat. **50**:330 (May) 1933.

The author has investigated the effect of banana powder on the stools of both normal infants and infants suffering from celiac disease. The present article has to do with normal infants only. Infants fed a mixture of two-thirds milk with the addition of 5 per cent banana powder showed a conversion of the intestinal flora from an almost complete gram-negative to an almost gram-positive state. This effect was produced within from twenty to thirty-five days. The changed flora in no instance could be mistaken for that found in the breast-fed infant, the predominant organism being Micrococcus ovalis. A possible explanation of the effect of banana powder on infant stools is the fact that fructose is the least well absorbed of the monosaccharides and offers an exceedingly favorable medium for the growth of Micrococcus ovalis and the gram-positive anaerobic intestinal bacteria.

WADDELL, JR., University, Va.

INFANT COLIC AS WE SEE IT. RAMSAY MOORE, Dallas M. J. **18**:130 (Oct.) 1932.

As minor causes of discomfort and colic in babies, the author mentions: (1) various types of cutaneous conditions, such as eczema, furuncles due to heat, and ammoniacal dermatitis; (2) umbilical hernias, a frequent cause of abdominal pain; (3) colds in the head with nose-block and earache; (4) otitis media; (5) constipation with resulting anal fissures; (6) cystitis and vaginitis with painful urination; (7) errors in nursing, such as overfeeding, irregular feedings, swallowing of gas and similar conditions; (8) teething, an occasional cause, and stomatitis.

Of the major types of colic, the author discusses: (1) hunger colic in 65 per cent of the sick babies, the majority of whom were breast fed; (2) hypertonia, or its more severe forms of gastro-enterospasm or pylorospasm (a result of disturbance of the sympathetic nervous system); of this second major type of discomfort, a hypothetic case is described and the treatment outlined; (3) thymic colic with symptoms identical with those of pylorospasm, with additional thymic symptoms such as cyanosis and stridor cough. Theories of etiology based on an allergic condition and a deficiency in calcium are briefly discussed.

The author states: "Success in recognizing and treating colicky infants depends upon a complete history of the case, a very careful physical examination, long and intelligent observation of the baby, extreme patience on the part of

the physician, complete elimination of assistance from the daddy, grandmother and neighbors and perfect co-operation on the part of the mother."

SMITH, Dallas, Texas.

THE DISTRIBUTION OF VITAMIN B COMPLEX AND ITS COMPONENTS IN THE PEANUT. F. W. SHERWOOD and J. O. HALVERSON, J. Agric. Research **44**:849, 1932.

Commercially blanched peanut splits, hearts and red skins and the corresponding raw products from selected Virginia Runner peanuts were tested for the presence of vitamin B complex by a method which does not differentiate between the components but in general favors the detection of the antineuritic fraction. The raw red skins contain the highest concentration of vitamin B complex, but there are appreciable quantities in the hearts and splits. The process of commercial blanching destroys a large part of the vitamin in the outer exposed red skins but does not have so marked an effect on that in the hearts and splits. Shelled raw kernels contain relatively much greater amounts of the antineuritic fraction than of the pellagra-preventing vitamin G.

KUGELMASS, New York.

THE EFFECT OF IRRADIATED ERGOSTEROL UPON THE ABSORPTION OF CALCIUM. N. B. TAYLOR and C. B. WELD, Tr. Roy. Soc. Canada **26**:9, 1932.

A series of 3 month old pups was put on an adequate diet of dog biscuit and meat, and the excretion of calcium was followed for twenty-eight days. At the end of this time irradiated ergosterol (0.12 cc. per kilogram, 250 D) was administered for thirty-one days; the rate of excretion of the calcium was nearly doubled. As the dose of ergosterol was increased to 2.1 cc. per kilogram there was a further rise in the excretion of calcium, while on the withdrawal of ergosterol the amount of calcium excreted dropped. No evidence was found that irradiated ergosterol increases the absorption of calcium; on the contrary, excretion is increased, even with small doses.

KUGELMASS, New York.

THE EFFECT OF SMALL (THERAPEUTIC) DOSES OF IRRADIATED ERGOSTEROL UPON THE SERUM CALCIUM. N. B. TAYLOR and C. B. WELD, Tr. Roy. Soc. Canada **26**:13, 1932.

The initial effect following either the oral or the subcutaneous administration of irradiated ergosterol was a temporary fall in serum calcium. This was followed by a rise. In one parathyroidectomized animal in which the serum calcium was below normal, the subcutaneous administration of one dose of ergosterol was followed by a further drop in calcium. Irradiated ergosterol, in doses of 1 cc. of 10,000 X, was used for oral administration, while 2 cc. of 10,000 X was employed subcutaneously.

KUGELMASS, New York.

THE EFFECT OF IRRADIATED ERGOSTEROL ON CALCIUM AND PHOSPHORUS RETENTION IN CHILDREN. C. B. WELD and J. F. SYKES, Tr. Roy. Soc. Canada **26**:81, 1932.

The calcium and phosphorus balances were determined weekly for ten weeks in six children, aged from 8 to 13 years, who were kept on a constant diet during that time. During the first five weeks in which determinations were made and for a month preceding, none of the children was given any vitamin D, while four of the six were given 50 Steenbock units daily during the last five weeks. The diet was a mixed diet of about 2,100 calories, containing about 0.8 Gm. of calcium and 1.18 Gm. of phosphorus daily. The small amounts of vitamin D given did not affect the calcium and phosphorus balances in normal children who were fed a diet moderately low in calcium but otherwise adequate.

KUGELMASS, New York.

CHEMICAL AND PHYSICAL PROPERTIES OF BURBOT-LIVER OIL AND ITS VITAMIN CONTENT. E. M. NELSON, CHESTER D. TOLLE and GEORGE S. JAMIESON, U. S. Dept. Commerce, Bur. Fish., Investigational Rep. **12**:1, 1932.

The liver of the burbot, Lota maculosa, yields from 30 to 56 per cent of oil, with a specific gravity of from 0.9236 to 0.9241, n. from 1.4787 to 1.4801, Hanus I no. from 165.3 to 172.4, acid value from 0.32 to 2.2 and unsaponifiable matter, from 0.8 to 1.0 per cent. Compound prepared oil is from three to four times as potent in vitamin D and from four to ten times as potent in vitamin A as good grades of medicinal cod liver oil. In general properties, the oil resembles cod liver oil.

KUGELMASS, New York.

FAT-SOLUBLE VITAMINS: THEIR SIGNIFICANCE IN NUTRITION. EDWARD MELLANBY, Edinburgh M. J. **40**:197 (April) 1933.

This lecture was delivered at the University of Edinburgh following the award of the Cameron prize for 1932. Mellanby has filled the chair of pharmacology at the University of Sheffield and has also been physician to the Royal Infirmary there for the past twelve years. He states that medicine owes much to the physiologist and biochemist but that the debt is not all on one side. He began the study of nutrition because of a request to study the calcium and phosphorus balance in a specific disease, rickets; although he saw numerous children who were suffering from rickets he thought that it was essential first to learn how to produce rickets in the animal. It took many months to learn the simple fact that with about 200 cc. of milk and unlimited bread or oatmeal gruel, rickets would be produced without fail in rapidly growing puppies from 6 to 8 weeks old. At the beginning removal of fat from the milk furthered the onset of the disease. In his earlier work he had two problems: first, whether vitamin A, which controlled growth in young rats, was the same substance which prevented rickets in the dogs; second, the explanation of the fact that some agent other than diet influenced the experimental results. The animals were allowed to run about freely in the open.

Mellanby's work has proved that cereals in themselves are rickets-producing substances. To overcome their harmful qualities and retain their good qualities abundant milk and vitamin D should be included in the dietary. Teeth have an advantage over bone in studies of the results of calcification in that they do not change their texture. Vitamin D is the chief but not the only important factor in dental and bone formation. There are interacting factors which may favor or interfere with the architecture of teeth and bones, and the early stages of calcification are the most important.

Teeth are better formed if breast feeding is not discontinued early and when there is an adequate intake of vitamin D as food or through the action of sunlight. Overfeeding of cereal and underexposure to sunlight result in a defective structure of teeth. Teeth are susceptible or resistant to caries, depending on their state of nutrition after formation.

In 1928 Green and Mellanby reported that in rats deprived of vitamin A infection developed in various regions. They therefore called vitamin A the anti-infective vitamin. As both a preventive and a curative factor diets rich in vitamin A have some value in certain types of human infection.

Experimental work shows that certain degenerations of the spinal cord and nerves may be caused by many dietetic factors including vitamin A, carotene and cereals. It is too early to conclude how much human infection and nervous disease are affected by vitamin A. The author presents photomicrographs showing the production and prevention of degenerative nerve lesions by the diet.

NEFF, Kansas City, Mo.

FEVER FROM DIETARY DEFICIENCY: THE TEMPERATURE IN AVITAMINOSIS C. G. MOURIQUAND, J. SCHOEN and M. POPOTAS, Compt. rend Soc. de biol. **108**:1121 (Jan. 8) 1932.

The authors quote opinions from the literature as to whether the fever in clinical scurvy is due to lack of vitamin C or to infection. They studied the rise and fall in the temperature of guinea-pigs during experimental scurvy. On the seventh or eighth day, the temperature began to rise progressively to from 38.5 to 39.5 C. (101.3 to 103.1 F.). When swollen joints were present, a temperature of 40 C. (104 F.) was sometimes reached. After the administration of vitamin C, the temperature rapidly fell to normal.

WAHL, Cleveland.

CALCIUM OF THE SPINAL FLUID AND EQUILIBRIUM OF THE BLOOD CALCIUM. C. GERNEZ and A. LESPAGNAL, Compt. rend. Soc. de biol. **108**:1260 (Jan. 8) 1932.

In eighteen patients of whom five were normal and the others had various clinical conditions, the calcium of the spinal fluid and blood was determined. The calcium in the spinal fluid averaged from 60 to 70 mg., and that in the blood, from 115 to 125 mg. per liter. The values remained constant in their relationship in all the patients studied.

WAHL, Cleveland.

ACTION OF CERTAIN CALCIUM DERIVATIVES IN EXPERIMENTAL RACHITIS IN THE RAT. RAOUL LLECOCQ and F. VILLUIS, Compt. rend. Soc. de biol. **109**:539 (Feb. 26) 1932.

White rats were fed an antirachitic diet. At the end of eight days, when rachitic signs were present, calcium salts were added: chloride, lactate, gluconate, carbonate, sulphate and monophosphate, biphosphate and triphosphate. It was found that improvement in the rachitic condition occurred when calcium phosphates were given even in small doses as compared to no effect with large doses of the other derivatives.

WAHL, Cleveland.

RICKETS. A. B. MARFAN, Nourrisson **21**:158 (May) 1933.

Marfan argues that rickets is not merely a disease of the bones and cartilage. He draws attention to the widespread involvement of the lymphatic tissue, including the tonsils, the anemia, the muscular hypotonia and the alterations in the spleen and the thymus. Exposure to ultraviolet rays brings about healing of the lesions of the bones, but does not improve the other disturbances. He believes that the fundamental cause of rickets must be a prolonged intoxication or infection and not merely a deficiency in minerals or vitamin D. Among the infectious diseases which cause rickets and which the author mentions are: congenital syphilis, tuberculosis (especially scrofula), bronchopneumonia, chronic infections of the skin, chronic nasal diphtheria and malaria. Auto-intoxication may be due (1) to prolonged gastro-intestinal disturbances, (2) to infantile scurvy or (3) to a prolonged dietary regimen which is lacking in the necessary minerals and vitamins.

Other etiologic factors in rickets are eclampsia in the mother and chronic nephritis (renal rickets) in the child.

MCCLELLAND, Cleveland.

METABOLIC STUDIES ON INFANTS: III. EXCRETION OF CREATININE AND BASAL METABOLISM. L. GAROT, Rev. franç. de pédiat. **9**:293, 1933.

The author used the technic of Janet and Bochet in cases of first degree hypothrepsia and obtained results similar to those of Benedict and Talbot. In second degree hypothrepsia he found considerable deviation from the normal, both plus and minus. In cases of this nature in which the excretion of creatinine

is normal the basal metabolism is similar to figures determined by Talbot and by Levine, namely, 71.8 calories per kilogram instead of the normal number, 52.9.

SANFORD, Chicago.

THE AMINO-ACIDS IN THE URINE OF ARTIFICIALLY FED INFANTS. M. GIUFFRÉ, Riv. di clin. pediat. **31**:298 (March) 1933.

Folin's modification of Schiff and Sorensen's method of determining the urinary amino-acids was used.

The urine of fourteen infants was studied; in several instances observations were made with the same infant when it was well and when it was sick with grip or diarrhea.

The elimination of amino-acids in the urine is greater in the infant than in the older child or in the adult, both in total amount and in percentage of total nitrogen. Infections, such as grip or diarrhea, were accompanied by an increased elimination of amino-acids. In undernutrition with atrophy, the excretion of amino-acids was less than normal.

HIGGINS, Boston.

FREQUENT CAUSES OF DYSTROPHIES IN NURSLINGS. S. E. BURGHI, Arch. urug. de med., cir. y especialid. **3**:108 (July) 1933.

The dystrophic state is produced by two fundamental mechanisms: first, insufficient alimentation of exogenous origin, as with poorly balanced or insufficient food, and second, insufficient alimentation of endogenous origin, as with faulty absorption. Infections will cause dystrophies in two ways: (1) by a diminution of alimentary toleration, and (2) by the production of toxemia.

SANFORD, Chicago.

STUDIES ON CHOLESTEREMIA IN EARLY INFANCY. ANTONIO G. VILLEGAS, Tesis de doctorado, Madrid, 1932.

This is an excellent article and should be read in full by any one interested in the subject. In brief, the author determined the normal amount of cholesterol in 122 infants. This was 1.3 Gm. per liter of blood. This is normal during dentition. Hypocholesteremia exists in tuberculosis, congenital syphilis, rachitis and severe nutritional conditions. Hypercholesteremia exists in the allergic form of tuberculosis, in convalescence from most diseases and in transitory, nonsevere digestive disturbances.

SANFORD, Chicago.

PROGRESS IN THE TECHNIC OF ARTIFICIAL FEEDING. L. SPOLVIRIM, Arch. f. Kinderh. **95**:278 (Feb.) 1932.

This study was undertaken in an attempt to modify the casein of cow's milk so that it might be better tolerated by the infant and more readily digestible. It is well known that the amount of casein in cow's milk is much greater than that in human milk and that the amount of lactalbumin is less; but it has not been hitherto appreciated that the lactalbumin acts as a protective colloid for the casein and that for this reason the casein of breast milk is in a much finer state of dispersion than that of cow's milk. It was found that acacia in a 5 to 10 per cent solution acts as a protective colloid for the casein of cow's milk, increasing the viscosity and lowering the surface tension.

Cow's milk so treated is well tolerated in concentrated formulas even by newborn infants. The emptying time of the stomach is shortened (one and one-half hours), and the stools resemble those of breast-fed infants, containing more fatty acids and less of the neutral fats and alkaline soaps. The experience of the author and his co-workers with this type of feeding has covered four years and extends to several hospitals and foundling homes. The results have been gratifying. The incidence of nutritional disturbances in foundling homes has definitely decreased.

LESLIE, Chicago.

EFFECT OF HYPERTONIC DEXTROSE SOLUTION GIVEN INTRAVENOUSLY. E. GYORGY and L. VESZELSZKY, Arch. f. Kinderh. **98**:164 (Jan. 24) 1933.

Infants were given a 40 per cent dextrose solution intravenously in amounts of 2 Gm. of sugar per kilogram of body weight. In well infants the values for blood sugar returned to normal within an hour and a half. The volume of urine voided depended on whether or not food had been withheld. In sick infants there was no apparent difference whether the stomach was empty or full. The following signs, which occurred in sick infants after the injection of dextrose solution, were considered to indicate a bad prognosis: reddening of the skin, cutaneous hemorrhages, a blood sugar value of over 600 mg. and failure of the blood sugar curve to return to normal within an hour and a half.

LEMASTER, Evanston, Ill.

EXPERIMENTS ON METABOLISM IN OLDER CHILDREN WITH A VEGETABLE DIET. FRANZISKA BOLDT, Arch. f. Kinderh. **98**:168 (Jan. 24) 1933.

Fifteen children, aged from 6 to 11 years, were fed a vegetable diet to which was added 1 Gm. of protein per kilogram of body weight a day. The daily intake amounted to 65 or 70 calories per kilogram. From 60 to 70 per cent of the nitrogen was retained. Of the total nitrogen excreted in the urine, 76.9 per cent was urea nitrogen. The values for ammonia in the urine were low. The diet definitely influenced the metabolism toward the alkaline side. Approximately 14.5 per cent of the calcium and 29 per cent of the phosphorus were retained. The author states that his results may be regarded as standard values for healthy children on a vegetable diet low in protein.

LEMASTER, Evanston, Ill.

IS RICKETS IN THE RAT A SINGLE CLINICAL ENTITY? WERNER KOLLATH, Arch. f. Kinderh. **98**:227 (Feb. 21) 1933.

Kollath discusses the symptoms and signs of rickets in the rat. The varied clinical and pathologic observations in rickets are thought to depend on the individual constitution, the function of the endocrine glands, the dietary elements, such as minerals, and a lack of vitamin D.

LEMASTER, Evanston, Ill.

INFLUENCE OF MAGNESIUM SALTS ON THE GROWTH OF RATS GIVEN A CONSTANT DIET OF CAROTENE. H. VON EULER and EBBA VIRGIN, Biochem. Ztschr. **249**:393, 1932.

When rats are given a diet of the proper qualitative components with sufficient vitamin A, the rate of growth may be affected by factors of any of the following groups: the three components of the vitamin B complex; the products of internal secretion, especially thyroxine, epinephrine and the sex hormones, of which that of the anterior lobe of the hypophysis is particularly important, and, lastly, inorganic salts, which act as catalyzers (manganese, iron, copper) or as regulators of the concentration of dibasic organic acids. Feeding of excessive amounts of magnesium salts causes general debility, osteoporosis or even slowing of growth. The influence of an overdose of these salts was investigated when the level of the intake of carotene was constant, the increase in weight and the changes in the epiphyses being used as criteria. With the smallest amount of magnesium (0.05 per cent of the basic diet) the maximum growth found with larger amounts was not attained. Maximum growth was obtained with 0.15 per cent and was maintained up to a concentration of 0.35 per cent, the growth diminishing gradually with still further increases in magnesium. Roentgen examination of the bones did not reveal any noteworthy changes.

KUGELMASS, New York.

EXPERIMENTAL THERAPY OF ALIMENTARY INTOXICATION. ROSENBAUM and YORK, Monatschr. f. Kinderh. **58**:191, 1933.

In animals made toxic by a combination of exsiccation and injection of endotoxin, neither oxygen nor cardiac and respiratory stimulants were of any value.

GERSTLEY, Chicago.

BLOOD PRESSURE IN EXPERIMENTAL ALIMENTARY INTOXICATION. CHASSEL, ROSENBAUM and YORK, Monatschr. f. Kinderh. **58**:211, 1933.

In experimental alimentary intoxication of animals produced by combined dehydration and endotoxin, the blood pressure shows a steady fall. In dehydration without endotoxin and in endotoxin poisoning without dehydration, the blood pressure is unchanged. There is no relation between lowered blood pressure and increased respiration.

GERSTLEY, Chicago.

THE VITAMIN C CONTENT OF MILK. B. BLEYER, München. med. Wchnschr. **80**:257 (Feb. 17) 1933.

The determinations of vitamin C were made by the chemical method described by Tillmans. Colostrum had the highest content of vitamin C. This gradually decreases, and after the first month of lactation remains fairly constant. The vitamin C content of human milk was at least twice that of good cow's milk. The values for vitamin C were fairly constant in human milk but varied considerably in cow's milk obtained on different days. Storage at high temperature and exposure to air destroyed the vitamin. This was avoided by keeping the milk in well filled, cooled, air-tight containers. Boiling milk at home destroyed only about 15 per cent of the vitamin C. Rapid pasteurization at high temperature was more protective to the antiscorbutic vitamin than prolonged exposure at a lower temperature. The addition of sugar (condensed milk) and acid (protein milk) aided in the preservation of vitamin C. Exposure of dried milk to ultraviolet rays destroyed some of the vitamin C.

BRAHDY, Mount Vernon, N. Y.

GLYCOGEN AND FAT CONTENT OF THE LIVER IN INTOXICATION OF INFANTS. H. C. GLOTZ, Ztschr. f. Kinderh. **54**:395, 1933.

The glycogen content of the liver of ten infants who died of intestinal intoxication varied between 1.4 and 4 per cent, which is relatively higher than is usually found in the livers of infants dying of other diseases.

In contrast to the depletion of glycogen of the livers of normal children after starvation, the livers of infants with intoxications are not so depleted. There is therefore no evidence of a disturbed carbohydrate metabolism in intoxication.

The fat content of the livers was found to be relatively lower than normal. No relationship existed between the concentrations of fat and glycogen and the duration of the illness.

SHELLING, Baltimore.

A NEW PROVITAMIN. A. ALFRED WINTERSTEIN, Ztschr. f. physiol. Chem. **215**:51, 1933.

The mixed pigments obtained by extraction with purified petroleum benzine of the peels from 2 Kg. of Gonocaryum pyriforme fruit shipped from the Dutch Indies were separated by chromatographic adsorption on fibrous aluminum oxide. The products were: lycopin, 10 per cent; A carotene and B carotene, from 20 to 25 per cent, and a new pigment, from 65 to 70 per cent. The last is a carotenoid with absorption bands and adsorption behavior intermediate between those of carotene and lycopin. It has antixerophthalmic activity and probably contains at least one ionone group in the molecule.

KUGELMASS, New York.

SUBCLINICAL DEFICIENCY DISEASES. G. MOURIQUAND, Acta pædiat. **13**:369 (June 6) 1932.

Insufficiency of various vitamins in the diet, often of more than one vitamin at a time, may produce confusing syndromes without causing classic deficiency diseases. The author introduces a complex vocabulary without clarifying the clinical issues.

MCINTOSH, New York.

PRESCORBUTIC ANEMIA. P. ROHMER and J. J. BINDSCHEDLER, Acta pædiat. **13**:399 (June 6) 1932.

Anemia was present in seven of fifteen cases of scurvy observed by the authors. In two of the seven cases the anemia was not relieved by the addition of vitamin C, but yielded when medicinal iron was given.

Iron and vitamin C (sometimes as lemon juice and sometimes as a powdered preparation made from cabbage) were given to dystrophic infants in whom no scurvy was manifest. In some cases in which one factor alone had little or no effect the two together cured the anemia. When the anemia failed to respond, there was some infection which interfered with the cure. It is not possible to determine from these observations whether the beneficial effect claimed for vitamin C was due to the vitamin or to an associated substance such as copper.

McINTOSH, New York.

ALKALINE RESERVE OF THE BLOOD PLASM OF CHILDREN, ESPECIALLY OF THOSE WITH EXUDATIVE DIATHESIS. P. C. GUGELOT, Nederl. tijdschr. v. geneesk. **76**:4844 (Oct. 15) 1932.

The author made an extensive examination of the alkaline reserve of the blood plasm in sixty-nine children with various diseases. He used the micromethod of Mook. The mean value of the alkaline reserve of the children, all of whom were fed the normal diet of the hospital, was 54.2 cc. per hundred cubic centimeters of plasma; age had no definite influence. There was little evidence of pronounced acidotic influence due to tuberculosis, although this had been found by other investigators. In eight children who showed symptoms of exudative diathesis, there was a small but constant decrease of alkaline reserve; the mean value was 48.9; these children showed no ketosis. A diet poor in salt (after Hermannsdorfer) effected a slight increase of the alkaline reserve, but without producing an acidotic influence, as has been contended by other investigators.

VAN CREVELD, Amsterdam, The Netherlands.

Prenatal Conditions

THE METABOLISM OF IRON IN THE ANEMIA OF PREMATURE INFANTS. CHARLES E. SNELLING, J. Pediat. **2**:546 (May) 1933.

After making studies of the iron balance and the excretion of pigment in a series of premature infants, the author draws the following conclusions:

1. Premature infants tend to have a positive iron balance when fed according to the method commonly employed.

2. The excretion of pigment is not excessive.

3. The anemia affects the red blood cells and the hemoglobin equally, develops in spite of treatment and improves spontaneously.

4. The anemia appears to be due to failure to utilize the available supplies rather than to lack of the substances which compose hemoglobin.

5. An etiologic hypothesis which would explain many of the observed phenomena portrays failure of utilization of the substances which compose hemoglobin, owing to an inadequate medullary space coincident with the premature cessation of hematopoietic activity in the liver.

LeMASTER, Evanston, Ill.

THE RÔLE OF UPPER RESPIRATORY INFECTIONS AS A CAUSE OF DEATH IN IMMATURE INFANTS. A. B. SCHWARTZ, Wisconsin M. J. **32**:77 (Feb.) 1933.

Prematurity with associated conditions continues to be the most common cause of death among infants. Efforts to lower the mortality have met with little success. Numerous deaths resulting from improper feeding or from infection have been listed under the vague term congenital debility. The freedom from or the occurrence of infections determines whether a great number of these immature infants live or

die, and the problem belongs to the field of preventive medicine. The factor of infection is not sufficiently appreciated in the provisions made for handling these small infants.

In a hospital to which only infants with nutritional cases were admitted, 89 immature infants were admitted during a ten year period. Excluding the 15 deaths that occurred within forty-eight hours after admission, there was a mortality of 42 per cent, 25 per cent of which represented deaths following infections of the upper respiratory tract. Of 157 immature infants who were admitted to a children's hospital of the usual type but who were kept in a separate room where individualized technic was carried out, there was, exclusive of the first forty-eight hours, a mortality of 57 per cent, 45 per cent of which could be ascribed to infections of the upper respiratory tract. A large number of the factors developed after admission to the hospital.

Because of the danger of infections of the upper respiratory tract, children's hospitals are not ideal locations for the care of immature infants. The obstetric floor of a general hospital or supervised homes using the Speedwell technic should give a lower incidence of respiratory infection and a lower mortality among immature infants.

JANNEY, Milwaukee.

STILLBIRTHS IN WISCONSIN FOR 1930. L. W. HUTCHCROFT, Wisconsin M. J. **32**: 197 (March) 1933.

Assuming that all stillbirths after the fifth month of gestation were reported, the ratio was 1 stillbirth for each 33 live births. The yearly number of stillbirths in Wisconsin is between 1,600 and 1,700, instead of 2,500, which it would be if the rate was that of the area of birth registration. There is a close relationship between stillbirths and deaths occurring during the first week after delivery.

Statistics based on the estimations of Williams and of the department of health of New York City show that syphilitic infections cause almost 400 stillbirths in Wisconsin per year, most of which are preventable. Statistics based on autopsy reports reveal that injury at birth is a large factor in 16 per cent of the stillbirths, yet only 4 stillbirths were ascribed to this cause in 1930. In 27 per cent of the stillbirths reported, no reason was given for the child being born dead. It seems probable that a large number of these deaths were due to intracranial injury. The following important causes were given for the stillbirths: toxemias of pregnancy, including nephritis, 4.7 per cent; malformations, 10.8 per cent; placenta praevia and placental disease, 7.4 per cent; abortions, miscarriages and premature births, 17.5 per cent; prolapse and compression of the cord, 8.2 per cent; malpresentations, deformed pelvis and difficult labor, 11.6 per cent.

The rate for stillbirths has shown no decline since 1910, although infant mortality has been reduced more than 50 per cent. In the period reviewed, stillbirths were relatively more numerous among males, and the rate for illegitimate children was nearly double that for legitimate children. The rate for Negroes was about the same as for white persons, but that for Indians was nearly double the rate for white persons. In rural areas the rate was 10 per cent lower than for urban districts. The rate was lowest among mothers giving birth to a second child, but it increased with each successive birth, so that the first and seventh pregnancies were followed by an equal number of stillbirths. The rate was lowest when the mother was between 20 and 29 years of age.

JANNEY, Milwaukee.

A DESCRIPTION OF A HUMAN OVUM FIFTEEN DAYS OLD, WITH SPECIAL REFERENCE TO THE VASCULAR ARRANGEMENTS AND THE MORPHOLOGY OF THE TROPHOBLAST. N. M. FALKINER, J. Obst. & Gynæc. Brit. Emp. **39**: 471, 1932.

The author describes an ovum obtained thirty-two days after the first day of the previous menstrual period, nineteen days after the calculated day of ovulation and fifteen days after the last coitus.

He noted that the features of the decidua of an ovum 15 days old do not completely correspond with those found in a premenstrual endometrium, in that the secretory activity of the glands and of the surface epithelium is more marked and the cells of the stroma do not resemble decidual cells, as they do in the premenstrual phase. He also observed that the vascular arrangement in the compact layer is unusual in demonstrating a proliferation of endothelial cells lining the capillary walls and a remarkable accumulation of leukocytes.

Falkiner further noted that the capillaries of the uterine circulation communicate with the endometrium at two different levels: the compact layer and the spongy layer. Thus, during placentation, when the compact layer is destroyed, circulation in the spongy layer continues uninterrupted. Falkiner believes that this uninterrupted circulation reduces the occurrence of thrombus formation, which would probably develop if all the capillaries were involved during trophoblastic invasion, and also that this persisting circulation ultimately aids the establishment of circulation in the implantation cavity. Since blood was not present in the implantation cavity of the specimen obtained, Falkiner believes that even as early as two weeks after impregnation a definite circulation is effected through the implantation cavity.

After studying the trophoblast, the author concludes that it is made up of four types of structure: cells of the Langerhans layer, a syncytial covering, strands in the necrotic zone and cells outside the necrotic zone.

ADAIR and MICHEL, Chicago.

A CASE OF CONGENITAL EPULIS. G. ARDOIN and M. COMBY, Arch. de méd. d. enf. **36**:228 (April) 1933.

Only twelve cases of the form of congenital tumor mentioned in the title have been recorded. The authors report an instance in a baby girl who presented at birth a bilobed, nonpediculated tumefaction, the size of a pea, on the superior maxillary border to the right of the medial line. No other abnormality was discovered; ablation was practical on the eighth day, and perfect healing was noted. Histologic examination confirmed in all respects the clinical diagnosis of epulis.

AMESSE, Denver.

CONGENITAL MALFORMATION OF THE HEART. DOUBLE MURMUR. MARQUÉZY, ROUGET and BOUSSOULADE, Bull. Soc. de pédiat. de Paris **30**:247 (April 19) 1932.

The case of a boy, aged 7 years, was reported because of abnormal cardiac findings. He was first examined at the age of 1 month, when there was evidence of a cardiac anomaly. He had a systolic thrill, which was most marked in the left fourth interspace. There were a loud rough systolic murmur, which was best heard just inside the apex, and a diastolic murmur with its maximum intensity at the inner part of the left third intercostal space. The electrocardiogram showed normal deflections. A roentgenogram showed enlargement of the right side of the heart, prominence of the pulmonary arc and hypertrophy of the left ventricle, giving the appearance of a heart *en sabot*. The systolic murmur was probably caused by an interventricular septal defect, and the diastolic murmur by insufficiency of the pulmonary artery, which was probably associated with a small degree of stenosis. The boy had only slight cyanosis of the lips and cheeks and none of the extremities.

BENJAMIN, Montreal, Canada.

CONGENITAL ANKYLOSIS AND BONY FUSION OF THE PHALANGES: A FAMILIAL MALADY; A STUDY OF TWO CASES. J. PERVÈS, Rev. d'orthop. **19**:628 (Nov.-Dec.) 1932.

Two cases of congenital ankylosis are presented, in a man aged 40, and in his son, aged 12. From the history it is brought out that fusion of the phalanges had been present in at least one member of the antecedent family in every generation, as far back at least as the great-grandparents.

The x-ray picture of the father's hand showed that only two phalanges were present in each of the four fingers. The thumb had the normal number of phalanges, but fusion was commencing between the first and second phalanges. The two hands were affected in the same manner. The fingers appeared short and stubby. The fusion had not interfered with the man's occupation, that of a gardener. The x-ray picture of the boy's hand showed that the three phalanges were present, but that fusion was almost complete between the first and second phalanges of all the fingers but not of the thumbs. On comparison of the cases, it is clear that the father had a more advanced condition than the boy, but that both conditions were essentially the same, the one being the end-result of the other.

Such fusions are not exceptional. The author refers to the published case reports of other writers, the most recent being an article by Mouchet and Saint-Pierre (*Rev. d'orthop.* **18**:210 [May] 1931). RYAN, Vancouver, Canada.

CONGENITAL MALDEVELOPMENTS OF THE NOSE. B. LANG, Virchows Arch. f. path. Anat. **285**:93, 1932.

Two unusual examples of nasal maldevelopment are described, one of proboscis lateralis and one of Kundrat's cebocephalic form of arhinencephaly. In each there were multiple malformations in addition to the nasal one, to which special attention is given. In the case of proboscis lateralis, the left half of the nose was normally formed. The right half was represented by a short, sessile structure attached at the inner canthus of the right eye. The right nasal bone and the right nasal cavity were absent. There was a coloboma of the right lower eyelid. The intermaxillary bone was absent. In the case of cebocephaly a rudimentary nose with a single nostril had been formed. The following structures had not been formed: the horizontal and vertical plates of the ethmoid, the small wings of the sphenoid, the optic foramina, the vomer, the lacrimal bones, the intermaxillary bone and the nasal cavities. The frontal lobes of the brain were fused in the midline, with maldevelopment of the olfactory lobes and other parts of the brain. The endogenous and exogenous factors that may have a part in the genesis of such maldevelopment and the period of embryologic development at which the latter may arise are discussed. SCHULTZ, Chicago. [ARCH. PATH.]

CONGENITAL VERTEBRAL DEFORMITY WITH ABSENCE OF THE NECK. A. FELLER and H. STERNBERG, Virchows Arch. f. path. Anat. **285**:112, 1932.

In the fourth of a series of studies of congenital malformations of the vertebral column, the authors describe six cases of absence or shortness of the neck. Five of these occurred in fetuses and one in a woman who died at the age of 51 years. The anomaly was described by Klippel and Feil in 1912 and is referred to in the German literature as the Klippel-Feil syndrome. In the authors' cases there were various malformations of the cervical and upper thoracic vertebrae, including failure of development or rudimentary development with fusion of vertebrae. Common to all was a defect of the dorsal arches of the vertebrae, which continued upward into the occipital bone. The anomaly is ascribed to interference with the normal development of the primitive segments of the body; it manifests itself before cartilage has been formed in the anlagen of the vertebrae.

SCHULTZ, Chicago. [ARCH. PATH.]

A CASE OF PARIETOFRONTAL CRANIOPAGUS. C. BLUMENSAAT, Virchows Arch. f. path. Anat. **285**:140, 1932.

This unusual example of symmetrical double monstrosity, in which the twins were broadly united by their corresponding parietofrontal regions, is of interest because the children lived from February 2 to April 8. During life they exhibited distinct individualities. One had pneumonia and died eight hours before the other. Separation was considered, but roentgen examination revealed that the subdural

spaces communicated widely with each other. The two brains were in close apposition, being separated only by pia, the two layers of which were united in places. The brain of the twin who died first revealed histologic evidence of postmortem change.

SCHULTZ, Chicago. [ARCH. PATH.]

THE MINERAL AND WATER METABOLISM IN PREMATURE INFANTS. H. PAFFRATH and J. MASSART, Ztschr. f. Kinderh. **54**:343 (March) 1933.

Four premature infants were studied for periods of twenty-three, fifty-seven, sixty and sixty-three days, respectively. During these periods they were fed with human milk, buttermilk or a combination of the two. The results are summarized as follows: 1. The mineral balance depends on the mineral intake. 2. The "supermineralization" of bottle-fed, full-term infants also occurs in premature infants. 3. Calcium may be retained without retention of water. 4. Alkali and water storage go hand in hand, but alkali may be relatively retained without water during hunger and loss of weight. 5. The salt and water metabolism of the premature infant is like that of an adult with edema and unlike that of a full-term child.

SHELLING, Baltimore.

CONGENITAL DIVERTICULA OF THE ESOPHAGUS. J. P. SLOOFF, Maandschr. v. kindergeneesk. **2**:36 (Oct.) 1932.

The author describes a case of this rare condition. The diagnosis was made roentgenologically. At the age of 1 year the child had developed normally.

VAN CREVELD, Amsterdam, The Netherlands.

CONGENITAL MUSCULAR DEFECTS. J. E. SCHULTE, Nederl. tijdschr. v. geneesk. **77**:510 (Feb.) 1933.

The author describes a case of a congenital isolated defect of the right deltoid muscle, which is a rare condition. The clinical significance of this deformity is demonstrated by the description of a patient with an analogous muscular defect as a consequence of a neurotic muscular atrophy. The left major and minor pectoral muscles were absent. The roentgenogram of the left lung was much clearer than that of the right. A defect in development is accepted as the cause of this condition.

VAN CREVELD, Amsterdam, The Netherlands.

TYPICAL CONGENITAL HIGH POSITION OF THE SHOULDER. E. H. LA CHAPELLE, Nederl. tijdschr. v. geneesk. **77**:784 (Feb. 18) 1933.

So-called Sprengel's deformity, congenital high position of the shoulder, is always accompanied by deviations of the ribs and by malformations of the vertebral column. The author observed nine typical cases of the condition in one province of Holland where many cases of congenital dislocation of the hip and of other deformities were observed. The deformity may be explained as a retardation in development. Formes frustes may occur. The length of the clavicle has no significance as a cause of the typical high position of the shoulder.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the New-Born

CEREBRAL BIRTH CONDITIONS WITH SPECIAL REFERENCE TO THE FACTOR OF HEMORRHAGE. CLARENCE A. PATTEN and BERNARD J. ALPERS, Am. J. Psychiat. **12**:751 (Jan.) 1933.

The study includes thirty infants' brains that were removed post mortem as a routine, regardless of antemortem indications of a cerebral pathologic condition. Seventeen of these brains showed subarachnoid hemorrhage, and twenty-six revealed subependymal lesions. Of the infants whose brains showed subarachnoid

hemorrhage, seven were born at full term, and four were born at 7 months, four at 8 months and two at 6 months. Instruments were used in eleven cases, including two cesarean deliveries. In but two cases was the condition at birth described as "good," the other infants being "weak" or in "poor condition" or "stillborn."

The duration of labor had little to do with either the incidence or the extent of the hemorrhage. Nor did the type of presentation, the anesthetic or the instrumentation play a rôle. Invariably the general condition of these infants was poor at birth. It is justifiable to assume that the hemorrhages occur prenatally and have little to do with trauma sustained at birth. Their exact causation is difficult to state. Perhaps they are due to defective myelinogenesis.

JAHR, Omaha.

THE TEACHING OF RESPIRATORY AND ALLIED CONDITIONS WHICH CAUSE CYANOSIS IN THE NEW-BORN. RALPH M. TYSON, Arch. Pediat. **50**:97 (Feb.) 1933.

Attention is called to cyanosis as one of the most common abnormal signs in the new-born. The many and various etiologic factors concerned with cyanosis in the new-born are discussed, with emphasis on differential diagnosis. The author aptly points out that treatment depends on correct diagnosis. The value of newer methods of resuscitation of the new-born is emphasized.

WADDELL, JR., University, Va.

CAUSES OF INFLAMMATORY CONDITIONS OF THE HEART IN NEW-BORN INFANTS. KARL CHODOWSKI, Pediatria polska **13**:15, 1932.

The author gives an extensive discussion of inflammation of the heart observed at postmortem examination. He divides cases into two main groups, syphilitic and nonsyphilitic. In his experience, the syphilitic heart was rarely encountered post mortem. However, the most important inflammatory conditions of the heart are due to febrile diseases of the mother during gestation. They are classified as follows: acute bronchitis, influenza, pneumonia, acute rheumatic conditions and acute tonsillitis. The author claims that microscopic examination of the cardiac tissue is most important in making a diagnosis.

KRUPINSKI, Chicago.

IMPROVEMENT OF THE TRACHEAL CATHETER FOR OBSTETRICAL USE. H. FUJIMORI, Jap. J. Obst. & Gynec. **15**:493 (Dec.) 1932.

The length and diameter of tracheas were studied for three years; the subjects were infants on whom autopsies had been performed, and mature and new-born infants. It was found that the diameter of the usual tracheal catheter is greater than that of the usual trachea, which varies from 4.7 to 5.5 mm. The commonly used no. 10 Nélaton catheter has a diameter of 6.2 mm., which is 0.7 mm. larger than the greatest trachea found. It is advocated, therefore, that a no. 8 Nélaton catheter be used. It has a diameter of 4.8 mm. A glass trap for mucus was designed by the author; it is 5.5 cm. in length and lies between the catheter and a rubber tube which is inserted into the physician's mouth.

After a study of 2,989 subjects, a statistical result was obtained. During the year preceding the introduction of the catheter, 1,517 infants were delivered. During this period, the death rate due to asphyxiation was 24.44 per cent. There were 1,472 infants delivered during the following year. The death rate due to asphyxiation was 19.14 per cent. These percentages are based on the total death rate and not on the birth rate.

ADAIR and ARNOLD, Chicago.

TREATMENT OF THE UMBILICAL CORD AND A SIMPLIFIED NAVEL CLIP. B. H. JAGERROOS, Acta obst. et gynec. Scandinav. **12**:400, 1932.

The author describes a combined method for the treatment of umbilical cords. This method makes use of omphalotripsy by means of an omphalotribe; crushing

of the cord is combined with the use of a blunt clip. Strong pressure is exerted at the root of the cord to force out the mucoid material. Fine silk is used as a ligature in this crushed area. A blunt clip is then applied immediately above the cuff of the skin, and the cord is severed. Jagerroos has never noted disturbances in healing of the cord with this method and comments favorably on the rapidity with which shrinkage and healing of the stump occur.

ADAIR and MICHEL, Chicago.

Acute Infections

VACCINIA OF THE EYELIDS AND CONJUNCTIVA. M. L. FOLK and E. L. TAUBE, Am. J. Ophth. **16**:36 (Jan.) 1933.

The case reported by Folk and Taube brings the total of reported cases to ninety-nine. Two forms of the disease are recognized, a diffuse ulcerative, membranous blepharoconjunctivitis and a type showing a typical umbilicated vacciniform pustule. Both types may be found in the same person. In only twenty-five of the reported cases was the condition the result of homo-inoculation; in the others it resulted from contact, in mothers, nursemaids and vaccinators. The authors' experiments with rabbits show that mere contact of the margins of the lids with vaccine lymph or serum from the pustule without friction may cause vaccinia, whereas vaccinia of the skin of the lids is almost always preceded by trauma. The condition is apparently self-limited, and the prognosis is good, the cornea being involved in only about 10 per cent of the reported cases.

WIEDER, Milwaukee. [ARCH. DERMAT. & SYPH.]

PREVENTION OF SCARLET FEVER. THEODORE MELNICK, Arch. Pediat. **50**:158 (March) 1933.

Five hundred and fifty-one children were tested by the Dick test; in ninety-four the reactions were found to be positive. Ninety-one of these children were immunized with Dick scarlet fever toxin, receiving five injections at weekly intervals. The following precautionary measures were found valuable in reducing the severity of the reactions: (*a*) the administration of a mild laxative, preferably milk of magnesia, the night before the injection; (*b*) restriction of the diet to fruit juices, cereal water, tea and toast on the day of the injection, and (*c*) restriction of activities on the day of the injection, before as well as after the injection. The injection should be given in the latter part of the day, in the late afternoon or early evening, and preferably on Friday, or on a day preceding a school holiday, so that if a reaction should appear, confining the child to bed, there would be no necessity for absence from school.

Melnick believes that reactions such as headache, nausea, vomiting and abdominal pain were decidedly reduced when these precautionary measures were carried out.

WADDELL, JR., University, Va.

EARLY DIAGNOSIS OF WHOOPING COUGH, INCLUDING A STUDY OF 100 CASES. WARREN QUILLIAN, Arch. Pediat. **50**:192 (March) 1933.

One hundred cases of whooping cough from Quillian's office files are reviewed from the standpoint of early diagnosis. It is thought that the blood picture is of little value as an aid in early diagnosis. Attention is called to the apparent early initial leukopenia. The most constant blood finding appeared to be lymphocytosis. Recovery of the organism by the cough-plate method affords the most satisfactory means of early and accurate diagnosis, and Quillian believes that such bacteriologic diagnosis should be practiced.

WADDELL, JR., University, Va.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **48**:375 (April 14) 1933.

The incidence of meningococcic meningitis and scarlet fever was slightly higher from Feb. 26 to March 25, 1933, than during the corresponding four week period of 1932. All sections of the country showed a continued seasonal increase of measles. Smallpox, poliomyelitis, diphtheria, typhoid fever and influenza were reported at definitely lower levels than in 1932. The average mortality rate from all causes in large cities was 11.8 per thousand population, the lowest rate in the eight years for which data are available.

LEMASTER, Evanston, Ill.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **48**:499 (May 12) 1933.

The incidence of measles and scarlet fever during the period of March 26 to April 22, 1933, was slightly higher than that of the corresponding period of 1932. The number of cases of poliomyelitis, smallpox, diphtheria and influenza was definitely less than in recent years. Typhoid fever and meningococcic meningitis were reported at about the same level as in 1932. The average mortality rate from all causes in large cities was 11.3 per thousand population, the lowest for this period in the years for which comparable data are available.

LEMASTER, Evanston, Ill.

PREPARATION OF A SCARLET FEVER STREPTOCOCCUS TOXOID AND ITS USE IN ACTIVE IMMUNIZATION. M. V. VELDEE, Pub. Health Rep. **48**:549 (May 26) 1933.

A method is presented for the concentration of the toxin of the scarlet fever streptococcus whereby the toxin content is increased fourfold without any increase in nitrogen. This concentrated toxin is detoxified by the action of formaldehyde and by storage at 37 C. for about sixty days.

Tests on susceptible persons indicate that the toxoid may be given in three doses to children under 15 years of age without subsequent reactions except local erythema accompanied by induration in a few children, tenderness in a still smaller number and mild systemic symptoms in an occasional child.

Of 1,168 persons on whom the Dick test was made with 1 skin test dose of toxin one month after the last injection, 83.2 per cent gave negative reactions; of 494 persons tested again about eight months after the last injection of toxoid, 87 per cent gave negative reactions.

LEMASTER, Evanston, Ill.

ROCKY MOUNTAIN SPOTTED FEVER (EASTERN TYPE) IN THE SOUTHERN STATES: REPORT OF SIX CASES IN TENNESSEE. WILLIAM LITTERER, South. M. J. **26**:407 (May) 1933.

Two years ago Rocky Mountain spotted fever was unrecognized in the eastern and southeastern states. During the past year more than 150 cases have been reported east of the Appalachian Mountains.

It is possible that the disease was introduced into Tennessee by three foxhounds which were shipped from the vicinity of Helena, Mont., an endemic area of the western type of Rocky Mountain spotted fever.

A patient who died came to autopsy and presented typical pathologic changes, both gross and microscopic. The virus from 4 of 6 patients was recovered by the inoculation of guinea-pigs. Strain 1 has been maintained for 71 generations, strain 3 for 66 generations, strain 5 for 12 generations and strain 6 for 9 generations to date. No evidence has been obtained of cross-immunity between the virus of endemic typhus and the strains of the virus isolated in the 4 cases. Ticks (Dermacentor variabilis) collected from dogs within the neighborhood of 2 of the patients were macerated and inoculated into guinea-pigs in the attempt to isolate the virus. Negative findings resulted. No ticks of the variety of Der-

macentor Andersoni were found. Guinea-pigs immunized with the spotted fever vaccine failed to become infected with the viruses from cases 1, 3 and 6.

SCHLUTZ, Chicago.

THE CIRCULATORY FAILURE IN DIPHTHERIA AND ITS TREATMENT. FRANCIS IND, Practitioner **130**:497 (April) 1933.

Ind states that circulatory failure in diphtheria is due to vasodilatation, weakened cardiac output from the action of the toxin on the cardiac muscle and damage to the arterial wall. In his cases of diphtheria the author made frequent daily determinations of the blood pressure. During the first two days, while the exudate was forming, the pressure remained normal. Then a drop occurred in both the systolic and the diastolic rate, the former showing the greater reduction. The administration of antitoxin caused a fall in the blood pressure; the reduction was greatest when the antitoxin was administered intravenously. The author feels that only 12,000 units should be given, and that the intramuscular method should be used. The dose may be repeated if marked reductions in blood pressure have not occurred. By this method the readings for pressure are reduced by only about 10 points. The author uses and advises the administration of ephedrine at six hour intervals in maximum doses according to age. This, he feels, is a definite aid in helping to maintain adequate blood pressure. He suggests the use of alcoholic beverages for severe cases. The general supportive measures of rest and diet are discussed.

SAPPINGTON, San Francisco.

PRECIPITIN REACTIONS IN THE BLOOD OF RHEUMATIC PATIENTS FOLLOWING ACUTE THROAT INFECTIONS. BERNARD SCHLESINGER and A. GORDON SIGNY, Quart. J. Med. **2**:255 (April) 1933.

Precipitin tests were carried out on the blood serum of seventeen rheumatic and four nonrheumatic children. In each the serum was tested for its precipitin content during the acute nasopharyngeal infection and afterward at weekly intervals.

The authors report that the precipitin corresponds to the type of streptococcus responsible for the infection of the throat. A certain amount of formation of cross precipitin occurred. The formation of this antibody was found to be delayed until from the second to the fourth week after the onset of the pharyngeal infection, a period that is usually called the "silent period," between infection and rheumatic manifestations.

Detailed description of the technic used is given in the report.

BRADFORD, Rochester, N. Y.

COINCIDENT INFECTION WITH MEASLES AND TYPHOID FEVER. DUMONTET, Arch. de méd. d. enf. **36**:232 (April) 1933.

In discussing the well known antagonism existing between different species of pathogenic bacteria infecting coincidentally the same host, such as that noted, for example, with the streptococcus of erysipelas and the tubercle bacillus in lupus, Dumontet reports two interesting cases of concurrent measles and typhoid.

In the summer of 1926 four patients with a severe type of typhoid fever were under treatment at the Lafayette Preventorium. In November two of the patients were still in the hospital ward, a girl, aged 7, and a boy, aged 8; both cases were of a grave type. The first patient had hyperpyrexia with excessively foul diarrhea, and the second had frequent intestinal hemorrhages. By the first of December, however, the temperatures were normal and convalescence was apparently well established.

Toward the middle of December a child in another division of the institution fell ill with measles and was isolated at a considerable distance from the ward for patients with typhoid fever. The invasion was mild, and in three or four days the temperature disappeared. The patient felt well, and during the absence of the nurse

surreptitiously visited the patients who were convalescing from typhoid fever. This was not discovered until much later. Two weeks later the boy, who had been free from fever for a month, was suddenly stricken with fever and a few hours afterward sustained a severe intestinal hemorrhage. A recurrence of typhoid fever was suspected, but the following day a typical eruption of measles developed; with this exanthem the hemorrhages promptly ceased. The boy's general condition, nevertheless, was grave; bronchopneumonia supervened promptly, and the patient died the following week.

On the day following the onset of measles in the boy, initial symptoms of measles were found in the girl, and in this patient likewise the advent of the secondary infection was marked by bleeding from the bowel. With the appearance of the eruption the bleeding was arrested. Bronchopneumonia complicated the invasion in this instance also, but the patient finally recovered. It would appear that during the period of invasion of measles there was a sudden decline in the immunity acquired against typhoid fever but that during the course of the disease this immunity was rapidly reestablished. Dumontet believes that the onset of measles produces humoral phenomena comparable to but not identical with those seen in protein shock, which annihilate for the moment the normal reactions of the organism.

AMESSE, Denver.

GROWTH OF STREPTOCOCCUS AND STREPTOCOCCIC ENTEROCOCCUS ON CULTURES OF TOXIC DIPHTHERIA BACILLI. G. JOANNIDES, S. PARAGHERGHION and A. ANGELO, Compt. rend. Soc. de biol. **109**:1175 (April 16) 1932.

The authors inoculated diphtheria cultures with a virulent streptococcus and an enterococcus, and observed the growth over a period of four months. It was found that apparently the toxin of the diphtheria bacilli destroyed the streptococcus but that the enterococcus remained very resistant to the attack by the diphtheria toxin.

WAHL, Cleveland.

ETIOLOGY OF POSTVACCINAL ENCEPHALITIS. C. KLING, E. WASSÉN and J. FAAHRAEUS, Compt. rend. Soc. de biol. **109**:1337 (May 6) 1932.

Five cases of encephalitis developed as a result of vaccination against smallpox. The period of incubation was from twelve to fourteen days, and the encephalitis was present for from one to seven days. At postmortem examination there was found a leptomeningitis of varying intensity, extending in some cases beyond the anterior surfaces of the brain to the isthmus, and in other cases, to the spinal cord. Microscopically, perivascular infiltration was definite, and in some instances there were areas of necrosis. In all the cases, a round or globoid parasite or protozoan-like organism was recovered and grown on ordinary mediums. These organisms were recovered from the pathologic tissue.

WAHL, Cleveland.

MORPHOLOGY OF THE PARASITE IN THE NERVE TISSUE OF SUBJECTS HAVING POSTVACCINAL ENCEPHALITIS. C. KLING, E. WASSÉN and J. FAAHRAEUS, Compt. rend. Soc. de biol. **109**:1340 (May 6) 1932.

The parasite isolated in five cases of postvaccinal encephalitis is very pleomorphic. Several types are described. There are large forms which may be round or ovoid, pyriform or elongated; they measure from 8 to 12 millimicrons in length and from 5 to 6 millimicrons in width. Some have vacuoles and at least two large chromophilic granules in the protoplasm; others occur in pairs with adjacent polar granules. A filament is described as being attached to some of the forms. Small forms measuring from 2 to 4 millimicrons by 1 millimicron are seen in great numbers. They have characteristics similar to those of the larger, bipolar variety. The various forms designate stages in the evolution of the parasite.

WAHL, Cleveland.

RED CELLS AND IMMUNITY: ABSORPTION OF TOXIN BY THE RED CELLS. R. DUJARRIC DE LA RIVIÈRE and N. KOSSOVITCH, Compt. rend. Soc. de biol. **110**:284 (May 28) 1932.

Massive doses up to 30 cc. of diphtheria toxin were given intravenously to rabbits. In ten minutes the animals were bled. The red cells were washed several times with physiologic solution of sodium chloride. Guinea-pigs received injections of the serum and of the washed cells. The serum produced no untoward effects, but the cells produced death, with the characteristic pathologic lesions associated with diphtheria toxin.

In addition, red cells from different animals, including man, were mixed with diphtheria toxin in different concentrations, then washed thoroughly and injected into guinea-pigs. The same toxic effects were produced, though there was considerable variability with the cells of the different species.

These experiments tend to prove that the red blood cells absorb the diphtheria toxin.

WAHL, Cleveland.

ACTION OF ANTIDIPHTHERITIC SERUM APPLIED TO THE SKIN. A. BESREDKA, Compt. rend. Soc. de biol. **111**:859 (Dec. 16) 1932.

Antidiphtheritic serum in an ointment of petrolatum and hydrous wool fat was rubbed into the flanks of a rabbit. In a second animal, in a similar base, normal serum was introduced by friction. On the following day, in the opposite flanks, diphtheria toxin (from 0.5 to 1 cc.), incorporated in the same base, was rubbed into the skin. In the first animal, practically no local reaction occurred, while in the other (the control) edema, redness and induration occurred locally. This proves that the antidiphtheritic serum was absorbed into the circulation.

A second series of rabbits received injections of ether 0.000025 unit of diphtheria toxin or $.25 cc. of a suspension of a twenty-four hour gelatin culture of diphtheria bacilli; following this, at intervals of one hour, the antidiphtheritic ointment was rubbed into the skin of the flanks. The rabbits receiving the ointment up to an average of six hours after the toxin recovered. This shows that the absorption of antitoxin through the skin produced a curative effect, as compared with the passive immunity in the first experiment.

WAHL, Cleveland.

VACCINATION IN EARLY INFANCY. O. JELINEK, Arch. f. Kinderh. **99**:95 (April 28) 1933.

Vaccination of twenty-two infants from 9 days to 9 weeks old gave a successful reaction in seventeen. All of eight infants from 9 weeks to 6 months old were successfully vaccinated by the first inoculation. The course of the reaction was mild, but rather protracted. However, when nineteen of these infants were revaccinated from one to three months later, five again responded with the typical formation of pustules. The author advises against vaccination in early infancy because the immunity produced is not of sufficient degree or duration.

LEMASTER, Evanston, Ill.

VACCINE THERAPY AGAINST PERTUSSIS. JULIO SCHWARZENBERG LOBECK, Rev. chilena de pediat. **2**:513 (Nov.) 1931.

Curative vaccination is not capable of modifying simple pertussis and is particularly ineffective if the disease occurs in persons affected with various forms of constitutional diathesis. It does not prevent the onset of the various complications which commonly occur with this disease.

Other forms of therapy, such as the injection of various other vaccines and foreign protein therapy, have proved equally ineffective in the treatment of the disease.

The author advises against all forms of stimulating therapy and does not believe in the efficacy of the preventive vaccination against pertussis. He does not believe

that the curative vaccine in any way diminishes the intensity and duration of the cough or in any way prevents the onset of complications.

He has found it of some value in certain forms of pertussis if used early in the febrile stage and if the child's organism is fairly robust. It has also proved valuable in the treatment of pertussis complicated by grip. For debilitated patients and patients with various forms of constitutional diathesis, the author prefers hemotherapy above all other methods in the treatment of pertussis.

SCHLUTZ, Chicago.

ROENTGEN IRRADIATION OF DIPHTHERIA CARRIERS. URSULA KRÄTSCHELL, Arch. f. Kinderh. **99**:42 (March 21) 1933.

Seventy-one diphtheria carriers were treated by roentgen irradiation of the nose and throat. Cultures became negative in thirty-eight subjects and continued to be positive in thirty-three. These results are rather disappointing, as they are no better than those obtained by the use of antiseptic solutions. The author states that treatment of the patient by fresh air is probably the best method of therapy.

LEMASTER, Evanson, Ill.

RECURRENT MEASLES FOLLOWING AN ATTENUATED ATTACK: LENGTHENING OF THE INCUBATION PERIOD. C. BLUME, Arch. f. Kinderh. **99**:49 (March 21) 1933.

Seventy cubic centimeters of adult whole blood was injected into an infant, aged 11 months, four days after exposure to measles. Following an incubation period of twenty days there was an attenuated attack of measles of short duration, with very mild symptoms and a slight rash. Three months later the infant was again exposed to measles, but this time received no prophylactic injection. Typical measles developed within from twelve to fourteen days after exposure.

LEMASTER, Evanston, Ill.

CLINICAL CONTRIBUTION TO THE KNOWLEDGE OF GONORRHEA IN CHILDREN: I. EPIDEMIOLOGIC OBSERVATIONS. L. VON DOBSZAY, Arch. f. Kinderh. **99**:102 (April 28) 1933.

Of 17,000 children examined during a period of five and one-half years 0.8 per cent were found to have gonorrhea. Whereas the incidence of congenital syphilis is decreasing, owing to better prophylaxis during pregnancy, the frequency of gonorrheal infection in children appears to be on the increase. In attempting to determine the sources of infection, it was thought that in most of the instances the disease was contracted from other members of the family, but only in 16 per cent of the cases could such a history be elicited. The greatest incidence of gonorrhea in children occurred in the age group from 3 to 6 years, and it was in this same age group that the longest period of treatment was required to effect a cure. The local defense of the genital tract against gonorrheal invasion at this age is apparently less than at any other time. To test the duration of viability of the gonococcus outside the body, infected discharges were placed on metal and wooden objects, in urine and in feces, on linen cloth, etc., and cultures were taken at varying intervals. Cultures could be grown from urine after twelve hours, from feces after thirty-six hours and from other objects tested after intervals varying from thirty minutes to fifty-four hours. It is very probable that infection of children indirectly through contamination of toys, towels and the like is a frequent occurrence.

LEMASTER, Evanston, Ill.

CEREBRAL COMPLICATIONS FOLLOWING VACCINATION AND ACUTE INFECTIOUS DISEASES. H. A. GINS, Deutsche med. Wchnschr. **59**:677 (May 5) 1933.

For the past ten years attention has been called to occasional cases of encephalitis following vaccination. In the statistics for mortality from 1912 to 1920,

Gins could find only one case of encephalitis following vaccination. About 10,000,000 vaccinations were performed in Germany during this period. From 1920 on, however, the frequency of such cases increased, probably because encephalitis epidemica itself became more widespread in Germany. Between 1927 and 1930, Gins found eleven cases in which the reports at autopsy verified the diagnosis of encephalitis and in which the disease seemed to follow vaccination. However, about twice as many cases were reported as being clinically cases of encephalitis due to vaccination although autopsy proved this diagnosis to be erroneous. The author thinks that encephalitis occasionally occurs also after some of the acute infectious diseases; however, the reporting of these cases as encephalitis is not obligatory in Germany, and the death is listed as due to the original infectious disease. Gins therefore cannot give an estimate of the incidence of these diseases in combination with encephalitis. He thinks that the organism is the same as that which causes regular encephalitis epidemica. Children who are subject to convulsions are more in danger of acquiring encephalitis after vaccination than are those not subject to convulsions. Gins therefore suggests that children of this type should not be vaccinated until at least one year after their last convulsion.

KERESZTURI, New York.

EFFECT OF VARIATION IN THE COMPOSITION OF MEDIUMS ON THE GROWTH AND TOXIN FORMATION OF DIPHTHERIA BACILLI. J. NITSCH, Ztschr. f. Kinderh. **54**:470, 1933.

Ordinary and toxic strains of diphtheria bacilli were grown on synthetic mediums, and in some instances toxins were produced in vitro. The growth and formation of toxins were accelerated by the addition of peptone or hydrolyzed peptone to the medium.

Of the separate amino-acids, asparagine and cystine were effective in promoting growth and the formation of toxins; arginine and tryptophan were much less effective. Production of toxins occurred best in mediums containing cystine. Glycine induced poor growth but did not inhibit the production of toxins.

SHELLING, Baltimore.

ELECTROCARDIOGRAPHIC INVESTIGATIONS IN ACUTE INFECTIOUS DISEASES. F. S. P. BUCHEM and L. POLAK DANIELS, Nederl. tijdschr. v. geneesk. **76**:4318 (Sept. 10) 1932.

In the course of scarlet fever, diphtheria and typhoid fever, the authors often found transitory deviations in the T wave of the electrocardiogram, principally in the third derivation. The deviations appeared and disappeared during different periods of the illness. They are caused by lesions of the myocardium and are not related to other complications. An analogous study in patients with pneumonia confirmed this opinion.

VAN CREVELD, Amsterdam, The Netherlands.

ENCEPHALITIS AFTER SCARLET FEVER. P. J. DUINKER, Nederl. tijdschr. v. geneesk. **76**:4758 (Oct. 8) 1932.

The author describes a case in which encephalitis apparently developed after scarlet fever in a girl of 8 years. She died three weeks after the onset of the scarlet fever.

VAN CREVELD, Amsterdam, The Netherlands.

THE DOG AS A SOURCE OF INFECTION WITH WEIL'S DISEASE. A. KLARENBEEK and J. VOET, Nederl. tijdschr. v. geneesk. **77**:388 (Jan. 28) 1933.

For many years cases of Weil's disease have been observed in dogs in Holland. The condition is often accompanied by jaundice; in many cases nephritis dominates the picture. The authors conclude that in some cases of Weil's disease in man the possibility of the infection being caused by a dog must be considered.

VAN CREVELD, Amsterdam, The Netherlands.

BACILLARY DYSENTERY IN AMSTERDAM. A. C. RUYS, Nederl. tijdschr. v. geneesk. **77**:634 (Feb. 11) 1933.

Bacillary dysentery (Sonne) prevails in Amsterdam endemically. The Flexner type caused a small epidemic in the winter of 1931-1932 in a limited quarter of the town, but the epidemic did not flare up the next summer. In imported cases the condition was often of the Y type; it did not spread. After clinical healing the patients may remain carriers by infected feces for weeks. Infection by contact is probably the most important cause of spread.

VAN CREVELD, Amsterdam, The Netherlands.

SALMONELLA SUIPESTIFER INFECTION IN AN INFANT. S. VAN CREVELD and A. C. RUYS, Nederl. tijdschr. v. geneesk. **77**:1004 (March 4) 1933.

In an infant, one of twins, sent to the hospital because of bronchopneumonia, a suppuration of the right knee joint developed; from the material removed by puncture Salmonella suipestifer (Kunzendorf) could be cultured. Examination of the blood and feces also revealed this organism. The other twin, who had become ill about the same time, died soon after being sent to the hospital; the symptoms were mainly in the air passages. Facts concerning the epidemiology of this infection are given.

VAN CREVELD, Amsterdam, The Netherlands.

Chronic Infections

THE PRESENT STATUS OF THE SKIN REACTION IN TUBERCULOUS AND NON-TUBERCULOUS SUBJECTS. E. S. MARIETTE and E. P. K. FENGER, Am. Rev. Tuberc. **25**:357 (March) 1932.

Four thousand subjects were given an injection of old tuberculin in one arm and of a new protein substance known as human tubercle bacillus protein in the other. The latter substance is one of the metabolic products of the acid-fast bacillus which causes the cutaneous reaction in persons with tuberculosis. It may be obtained from different types of tubercle bacilli and from the timothy bacillus. This protein is identical with the original tuberculoprotein isolated by Seibert. From a comparison of the reactions observed in the four thousand persons tested, the authors conclude that human tubercle bacillus protein is as sensitive and as protective as old tuberculin and probably more so. In the doses recommended this new protein is safe. In large doses, however, the human tubercle bacillus proteins are not specific. There is apparently a protein substance common to all acid-fast bacilli, which, if given in large enough doses, will elicit the same type of reaction as that obtained from old tuberculin. The human tubercle bacillus protein is a better testing substance than old tuberculin, since it represents a substance in a purified form, which can be weighed out in milligram doses so that the exact milligram content of the solution is known.

EUGENE SMITH, Ogden, Utah.

THE PATHOGENESIS OF TUBERCULOUS MENINGITIS. ARNOLD R. RICH and HOWARD A. MCCORDOCK, Bull. Johns Hopkins Hosp. **52**:5 (Jan.) 1933.

Experimental and morphologic evidence is presented which demonstrates that diffuse tuberculous meningitis is not a direct and immediate result of hematogenous infection of the meninges. Miliary tuberculosis produces only rare, sparsely scattered tubercles in the meninges, not diffuse meningitis. Tuberculous meningitis has its origin in the discharge of bacilli into the cerebrospinal fluid from adjacent older caseous tuberculous foci. Such discharging foci were found, by careful search, in the substance of the brain or cord, in the meninges, in the bones encasing the central nervous system or in the choroid plexus in seventy-seven of the eighty-two cases of meningitis in this series. In all except two of these seventy-seven cases the demonstrated source of the diffuse meningitis was

in the substance of the central nervous system or in the meninges. In the five cases in which no local focus was found the material for study was incomplete.

LYTTLE, New York.

TUBERCULOSIS IN CHILDHOOD. M. POLLAK, Illinois M. J. **43**:278 (March) 1933.

Pollak believes that the chief characteristic of pulmonary tuberculosis in childhood is the latency of the disease. Therefore, only the systematic examination of patients apparently healthy previous to contact will lead to the finding of cases in the early stage of the disease. Tuberculin tests and roentgenograms combined are essential in the diagnosis. Air baths and heliotherapy are beneficial in the treatment of the juvenile type of tuberculosis. In the adult type, surgical treatment (artificial pneumothorax, phrenicectomy and other measures) should be resorted to when the involvement is advanced.

BARBOUR, Peoria, Ill.

CHEMICAL COMPOSITION OF THE ACTIVE PRINCIPLE OF TUBERCULIN: XVI. LOCAL CUTANEOUS SENSITIZATION (ARTHUS' PHENOMENON) PRODUCED IN NORMAL RABBITS AND GUINEA-PIGS BY THE PROTEIN OF TUBERCULIN. FLORENCE B. SEIBERT, J. Infect. Dis. **51**:383 (Nov.-Dec.) 1932.

Specific cutaneous sensitization identical with that produced by infection with live tubercle bacilli or by the injection of dead bacilli can be produced in rabbits and guinea-pigs by the injection of highly purified undenatured proteins of tuberculin.

TOOMEY, Cleveland.

TUBERCULOUS MENINGITIS. H. BROOKER MILLS, M. J. & Rec. **137**:330 (April 19) 1933.

Tuberculous meningitis is usually secondary to pulmonary tuberculosis in infants, and to involvement of the bones and of the lymph nodes in children. The human type of bacillus is found to be responsible in the majority of cases. The bovine type is the cause with increasing frequency as the child grows older and is not so closely associated with his parents. In 70 per cent of cases of tuberculous meningitis in children, a history of exposure to tuberculous adults may be obtained. The typical pathologic changes, symptomatology and physical findings and a report of three cases are given in the article. The prognosis is hopeless when the bacillus is found in the spinal fluid. The only treatment is repeated lumbar punctures in order to relieve the suffering of the patient.

WILLIAMSON, New Orleans.

EARLY DETECTION OF PULMONARY TUBERCULOSIS. HENRY D. CHADWITH, New England J. Med. **208**:1143 (June 1) 1933.

How much significance should be attached to a history of contact?

In the outpatient department of the Herman Kiefer Hospital about one thousand new patients are examined each month, and each one is questioned as to exposure to tuberculosis.

The principal reasons for delayed diagnosis are: Pulmonary tuberculosis may be present in well developed and well nourished persons without producing noticeable symptoms, and therefore they see no reason to consult a physician. When symptoms do appear, the patients delay and try home remedies, and so months may intervene before a physician has a chance to examine them. Physical examination may then not be revealing or conclusive, and the patient may be kept under observation for many months more. Palliatives are tried until definite signs appear or a positive reaction of the sputum is obtained. Therefore, when a defi-

nite diagnosis of tuberculosis is made the disease is usually far advanced. The presence of tubercle bacilli in the sputum usually means that the disease has progressed beyond the minimal stage.

A history of contact is of some diagnostic significance in children but not in adults.

Fatigue, loss of weight, poor appetite, frequent colds or cough lasting more than two weeks and spitting of blood are symptoms that demand investigation.

Classification as to Diagnosis and Contact

Adults	White	Colored	Total	Percentage
Number of adults	6,822	1,838	8,660	
Known contacts	3,077	839	3,916	45
No known contacts	3,745	999	4,744	55
Known contacts found tuberculous	455	135	590	15
No known contacts found tuberculous	1,042	341	1,383	29
Children				
Number of children	4,424	1,117	5,541	
Known contacts	2,378	711	3,089	59
No known contacts	2,040	412	2,452	44
Known contacts found tuberculous	412	157	569	19
No known contacts found tuberculous	249	80	329	13

The author suggests a tuberculin test for all children up to 15 years of age. Roentgenograms should then be taken of all children giving positive reactions. One should become skeptical of the value of the stethoscope in the diagnosis of pulmonary tuberculosis and put more faith in roentgen examination.

GENGENBACH, Denver.

THE BOVINE TUBERCLE BACILLUS IN HUMAN TUBERCULOSIS. A. STANLEY GRIFFITH, Brit. M. J. **2**:501 (Sept. 10) 1932.

The author gives a summary of the findings of the Royal Commission from 1911 to 1931 regarding tuberculosis in the British Isles, with special reference to the relationship between the human and the bovine type. It is stated that a large proportion of all tuberculous lesions—certainly those of the nonpulmonary form, such as cervical adenitis, meningitis and tuberculosis of the bones and joints—are due to the bovine infection. On the other hand, only approximately 2 per cent of pulmonary tuberculosis in England and Scotland is to be attributed to bovine infection. It is pointed out, however, on the basis of history and previous investigation, that children infected during early life with the bovine tubercle bacillus may in adult life have pulmonary tuberculosis due to the same bacillus. It is stated, further, that Koch's opinion that bovine tuberculosis has little importance for man has been decidedly disproved. The opinion is expressed that the bovine bacillus has a virulence for man at least as great as that of the human type. An outline is given of the author's recent investigation to prove or disprove the opinion previously formed.

Of eighteen cases of children dying from tuberculous meningitis, 33⅓ per cent were found to be of the bovine type. The author has recently found seven cases of pulmonary tuberculosis in addition to the previously reported ones in which only bovine bacilli were found in the sputum. Other authors have reported to him, though not certainly, additional cases. The possibility of mutation of bovine and human bacilli is discussed, and although experimentally such a change has not been demonstrated it is deemed possible that changes may arise during the progress of natural infection, for example, when bovine bacilli persist in the tissues of the human being into adult life, giving rise to chronic, slowly progressive tuberculosis. Although the accepted idea is that practically all tuberculosis is acquired during childhood, doubt is expressed by the author that this is true

in all cases, since bacteriologic and pathologic investigation does not bear out this idea as an absolute fact. The statement is made that bovine tubercle bacilli enter the body almost exclusively by way of the alimentary tract, and that milk is the usual vehicle of infection. Further, when adults acquire tuberculosis it is practically entirely by the human type of bacillus, which is inhaled rather than ingested. In some instances it is difficult to distinguish between the human and the bovine type, but that the type is mammalian rather than avian is undoubted. The author stresses the seriousness of the bovine type of tuberculous infection.

ROYSTER, University, Va.

THE RÔLE PLAYED BY BOVINE TUBERCLE BACILLI IN HUMAN TUBERCULOSIS. BRUNO LANGE, Brit. M. J. **2**:503 (Sept. 10) 1932.

A brief discussion and summary of the history of the discussion regarding the relationship between bovine and human tubercle bacilli are presented. The technic of differentiation is outlined, and the difficulties of conclusive differentiation are pointed out. Statistics are presented showing the incidence of bovine infection in man and all types of lesions in Germany. The author then compares his statistics with those for Scotland and England.

The various types of lesions differ in their incidence in different parts of the same country and in different countries, and it is especially noticeable that the bovine type is more important in dealing with children than with adults. The author doubts that the bovine type is a decided menace, certainly so far as Germany is concerned. The relative dangers of the two types and the incidence of infected cattle are discussed. Then follow rules pertaining in certain parts of Germany for the extermination of the bovine type, together with the results obtained by these methods. An important phase of the movement is the inspection of milk along lines outlined. The importance and necessity of continued research are emphasized.

ROYSTER, University, Va.

TUBERCULIN IN DIAGNOSIS. S. LYLE CUMMINS, Brit. M. J. **2**:1089 (Dec. 17) 1932.

The author discusses the value of tuberculin in the diagnosis of tuberculosis in adults, in children and in infants, with special reference to the significance of positive and negative reactions in different age groups.

ROYSTER, University, Va.

HEMOPTYSIS: FOR DIAGNOSIS. ? EPITUBERCULOSIS. ALAN MONCRIEFF, Proc. Roy. Soc. Med. **26**:510 (March) 1933.

A boy, aged 4½ years, had an attack of acute hemorrhagic nephritis following acute tonsillitis. Two months later he was admitted to the hospital because he had a temperature of 100 F. His breath was offensive, and he coughed up offensive sputum for two days during his stay in the hospital; however, he gained in weight and felt well. Three months later, he was brought back because he had coughed up about 2 tablespoonfuls of blood. No physical signs were found in the lung at the time. A week later, the breath sounds were weaker in the right axilla than in the left, and the percussion note was impaired. Roentgen examination showed that the process in the lung was extending. The fingers were slightly clubbed. The Mantoux reaction was strongly positive. The interest in this case is that the child's general condition remained good while the process in the lungs spread quickly. Since the Mantoux reaction was positive, the diagnosis of epituberculosis seemed most likely. An alternative hypothesis was bronchiectasis as a result of inhalation of septic material at the time of the tonsillectomy.

WILLIAMSON, New Orleans.

ACTINOMYCOSIS OF LUNG. R. W. B. ELLIS, Proc. Roy. Soc. Med. **26**:513 (March) 1933.

In August, 1932, a boy of 5 years was seized with pain in the right side of the chest, and was kept in bed for two or three weeks. He made a good recovery, but cough persisted and there was some dyspnea on exertion. In December, a fluctuant swelling was noticed on the right anterior wall of the chest. The patient was admitted to the hospital with a temperature of 104 F., a respiratory rate of 40 and a pulse rate of 130. The percussion note was somewhat impaired over the apex of the right lung and was dull over the rest of that lung. The swelling was incised and drained, and yellowish, blood-stained pus was evacuated. Examination of pus showed yellow granules the size of a pinhead with numerous filaments of gram-positive streptotrix in the film, which was typical of actinomycosis, and grew anaerobically on culture. Roentgen examination showed a homogeneous opacity at the base of the right lung, with marked thickening of the pleura over the whole of the lung. Roentgenograms taken after the injection of iodized poppy-seed oil 40 per cent showed considerable deformity and obstruction in the bronchi of the middle and lower lobes of the right lung. There was no evidence of bronchiectasis. The father of the patient was a painter, and the patient had no known contact with cattle or grain, or with any farm or dairy worker.

WILLIAMSON, New Orleans.

CHOROIDAL TUBERCLE IN MILIARY TUBERCULOSIS WITHOUT MENINGITIS. G. G. OENMAN and E. WOLFF, Proc. Roy. Soc. Med. **27**:315 (Jan.) 1933.

The author reports a case in a child aged 8 months. There was no history of tuberculosis in the family. On examination there were an impaired percussion note and bronchial breathing at the base of the left lung. The Mantoux test was positive. The temperature rose. Tubercle bacilli were found in the sputum and in the stool. In the fundus of the left eye was a yellowish, ill defined, rounded and slightly raised area about half the size of the disk. This was reported as a choroidal tubercle. Postmortem examination revealed no meningitis. There was extensive caseating tuberculosis of both lungs, with cavities in the lower lobe of the left lung. There were caseous glands in both lungs and miliary tuberculosis of the abdominal viscera.

WILLIAMSON, New Orleans.

ARTIFICIAL PNEUMOTHORAX IN TUBERCULOSIS IN THE CHILD. DR. ALFREDO BLAYA, Arch. d. hosp. de niños, Roberto del Rio **3**:146 (Sept.) 1932.

The induction of artificial pneumothorax in the child during the school age is as feasible as it is in the adult. It is indicated in subjects in whom the tuberculous lesion is of a unilateral exudative type, with the presence of tubercle bacilli in the sputum, or when the lesion is of the cavernous type. It is especially useful in certain cases in which the cavernous lesion is accompanied by hemoptysis. The procedure shortens the time required for the evolution of the lesions in pulmonary tuberculosis, suppresses considerably the bacillus-laden sputum and makes this type of person much safer for his environment. Pleural adhesions may prevent total collapse of the affected lung, but repeated pneumothorax may overcome this hindrance.

SCHLUTZ, Chicago.

ERYTHROSEDIMENTATION IN TUBERCULOSIS OF INFANCY. Z. PINTO, P. NOGUEIRA, R. PERIERA, L. ESCALANTE, B. SANCHEZ and J. M. PÁEZ, Arch. de med. inf. **1**:221 (Sept.) 1932.

The authors studied the methods of Castillo, Westergreen and Lienzenmeier. Westergreen's method is the easiest, but all the methods are applicable, and the findings are similar. It was found that the phenomenon of erythrosedimentation was not specific for tuberculosis. There is, however, some relation between the intensity of the reaction and the state of the lesion. It decreases with recovery

and increases with further advancement. It can be employed as a guide for tuberculous activity. It sometimes disappears before death. The authors followed these observations with studies on the indexes of Arneth, Velez and Panza-Duco. They did not find that these indexes had the positive values attributed to them by their authors. SANFORD, Chicago.

EXPERIENCE WITH ACETARSONE IN CONGENITAL SYPHILIS. BAUMBACH, Arch. f. Kinderh. **99**:151 (May 30) 1933.

This clinical report deals with the results observed in sixty-one infants with congenital syphilis who were treated with acetarsone by mouth. The series was divided into three groups. The first group received the rapid treatment with acetarsone, consisting of daily doses of the drug for six weeks at each course. The intermittent treatment with acetarsone, which was given to the second group, consisted of twelve week courses in which the drug was given for periods of one week alternating with periods of one week with no medication. The third group was treated by the combined method, in which mercurial ointment was administered by inunction for one week followed by acetarsone for one week, and the two methods of therapy were alternated for a total of twelve weeks. In all three groups rapid improvement in symptoms, physical signs of syphilis and general health occurred during the first few weeks of treatment. Serologically, the best results were obtained by the combined treatment, with which two thirds of the patients gave negative reactions to the Wassermann test after the first course. There were eighteen deaths—ten from pneumonia, three from sepsis, one from dyspepsia and four from the syphilitic infection directly. In no instance was any injurious effect attributed to acetarsone. LEMASTER, Evanston, Ill.

TREATMENT OF TUBERCULOSIS BY PNEUMOTHORAX. K. KLINKE, U. PETERSON and H. SKALETZ, Monatschr. f. Kinderh. **58**:169, 1933.

One hundred and twenty-two children with various types of tuberculosis were kept under observation for periods up to fifteen years. The treatment employed was pneumothorax. The authors conclude that in the phthisis of puberty, pneumothorax is preferable to conservative therapy. In other types of tuberculosis, such as the secondary pulmonary and the disseminated forms and even the primary infiltrations and epituberculosis, the results are indefinite. GERSTLEY, Chicago.

TUBERCLE BACILLI IN THE STOMACH CONTENTS. D. SCHYLLA, Monatschr. f. Kinderh. **58**:218, 1933.

In fifty-five children reacting positively to tuberculin tests, tubercle bacilli could be isolated from the gastric contents of thirteen. In the cases of inactive tuberculosis, bacilli were found only after repeated investigations. They were so rare that the author believes there is ordinarily little danger of contagion in these inactive cases. GERSTLEY, Chicago.

Internal Diseases

CHRISTIAN'S SYNDROME. R. S. JASON and S. V. ABRAHAM, Am. J. Ophth. **14**:1146 (Nov.) 1931.

The authors give a short history of Christian's syndrome and review the literature on the subject. They report the case of a child first seen at the age of 1 year and observed for over two years. She was normal up to the age of 8 months, when proptosis of the right eye occurred. Roentgen examination revealed lesions of the bones of the skull, and the child had loose teeth and gingivitis. The bone lesions improved under treatment with radium, although the authors question whether this improvement was due to the radium since in other reported cases

there was improvement without treatment. A section of bone was removed and studied. The absence of polyuria and polydipsia is explained by the lack of bony changes in the sella. The author remarks the lack of uniformity in the histologic appearance in the different cases reported, and concludes that the diagnosis should be made mainly on the clinical and roentgen findings.

REESE, Philadelphia. [ARCH. OPHTH.]

INTESTINAL PARASITISM: DIAGNOSIS AND TREATMENT. DAMASO DE RIVAS, Am. J. Trop. Med. **12**:477 (Nov.) 1932.

De Rivas discusses briefly the diagnosis of intestinal parasitism from the point of view of the clinic and the laboratory, and outlines in detail his plan of treatment.

The preparation of the patient consists in emptying the intestinal tract and passing the tube into the duodenum. The patient is then ready for treatment, which consists in the injection of from 1 to 2 ounces (30 to 60 cc.) of a warm glycerosulphate solution, according to the age of the patient, followed in about five minutes by an injection of 500 cc. of a physiologic solution of sodium chloride at a temperature of from 45 to 47 C. (about 113 to 117 F.) into the duodenum. This is allowed to flow at the rate of from 100 to 150 cc. per minute. At intervals of two or three minutes the irrigations are repeated, until 1 or 2 liters has been given. After this the patient is allowed to rest.

In the treatment of parasitism in the large intestine, the patient is prepared in the same manner and is given, in addition, colonic irrigations of a 1:5,000 solution of copper sulphate at a temperature of from 45 to 47 C. (about 113 to 117 F.), at the rate of from 100 to 150 cc. a minute. If there is discomfort, the colon is emptied, and the irrigation is started again when the symptoms subside.

The number and frequency of treatments necessary to effect a cure depend on whether the condition is a metazoan or a protozoan infestation. In metazoan infestation one treatment may be sufficient, while in protozoan infestation de Rivas recommends treatment every other day for two weeks, twice weekly for the next two weeks and weekly until repeated examination of the feces shows nothing abnormal. With this type of treatment he reports excellent results in cases of intestinal parasitism.

BURPEE, Augusta, Ga.

PULMONARY INFECTIONS BY THE FRIEDLÄNDER BACILLUS (BACILLUS MUCOSUS CAPSULATUS). FRANK FREMMEL, KARL J. HENRICHSEN and HENRY C. SWEANY, Ann. Int. Med. **5**:886 (Jan.) 1932.

The history of Friedländer's bacillus and its rôle in the production of pneumonia are reviewed, and a case of pneumonia due to this organism occurring in a man, aged 49, who lived only twenty-six hours after the onset is reported.

From 1 to 8 per cent of cases of pneumonia are said to be caused by the organism.

There is a peculiar clinical course with sudden death and characteristic gross and microscopic appearances of the tissues involved. The mortality rate is high.

The clinical course is not always regular. Usually the onset is sudden, without chill; there is no herpes of the lips, and death occurs suddenly between the second and the fifth day, usually before the third. Occasionally the disease resembles lobar pneumonia, except that it usually terminates more suddenly. The physical signs are those of engorgement rather than hepatization. There are signs of dulness with suppression of breath sounds and an absence of subcrepitant râles. This is perhaps due to the large numbers of encapsulated bacilli which fill the alveoli and finer bronchi with a sticky mucoid material preventing the passage of air.

Occasionally there is a tendency to chronicity, though usually the disease is fatal.

The most important pathologic observations are the pseudolobar consolidation due to dense confluence of bronchopneumonic foci (rarely lobar), the absence of a red stage of hepatization, the mucoid exudate on the cut surface, the scarcity

and irregularity of the red cells and fibrin within the alveoli and the presence of a moderate number of monocytes containing large numbers of encapsulated bacilli.

Hyperemia and thrombosis of the alveolar vessels lead to necrosis and the formation of abscesses if the patient survives sufficiently long.

The chronic form may resemble tuberculosis. WILSON, Norfolk, Va.

CELIAC DISEASE. SIDNEY V. HAAS, J. A. M. A. **99**:448 (Aug. 6) 1932.

Celiac disease is not generally known to occur at all ages. The pathogenesis is obscure, but apparently it is likely to follow a heavy carbohydrate diet, and there seems to be a familial predisposition to the disease. Bacillus bifidus predominates, and at the height of the disease there is a diminution in the number of colon bacilli. The successful treatment of celiac disease is based on recognition of the fact that carbohydrates in the usual forms must be excluded, that milk must not be used, and that fats, especially cod liver oil, must be excluded at the beginning of the treatment. BONAR, Salt Lake City.

THE MANAGEMENT OF HEMORRHAGIC PROBLEMS IN INFANCY AND CHILDHOOD. I. N. KUGELMASS, J. A. M. A. **99**:895 (Sept. 10) 1932.

Hemorrhagic disturbances are associated with many diseases, rarely conform to pictures in textbooks and are produced by varied causes. The hemorrhagic status of a patient may be stated clinically in terms of degree of function of the vascular endothelium and its blood content. The clotting component or a vascular alteration is the controlling factor on which a diagnosis is dependent. There is a low index of blood-clotting function in potential hemorrhagic disturbances which can be accelerated by a dietary regimen high in protein and fat. Oral administration of gelatin solution may prevent potential hemorrhagic disease of the new-born infant, as will antepartum institution of a diet productive of clotting. Hemophilia can be definitely diagnosed and controlled therapeutically but not cured by protein desensitization. The author has had no success with injections of female sex hormone preparations alone or reinforced with anterior lobe pituitary extract. Avitaminosis causes degeneration of the vascular epithelium in scurvy, marasmus and Herter's infantilism. Deficiency of vitamin C and of vitamin B (or F) has been shown to injure the vascular endothelium and thus produce hemorrhagic manifestations. Erythema multiforme, Schönlein's purpura and Henoch's purpura have a common allergic basis in that children with these conditions show an increased capillary permeability from foods or bacterial proteins. Treatment consists of removal of the offending allergen. BONAR, Salt Lake City.

SICKLE CELL ANEMIA. W. W. ANDERSON and R. L. WARE, J. A. M. A. **99**:902 (Sept. 10) 1932.

There have been only sixty cases of sickle cell anemia reported since John B. Herrick first described the disease. It is a disease of childhood, usually affecting the colored race exclusively, with definite familial tendencies. The pathologic process is limited to the liver, spleen and bone marrow, all of which structures are permeated with large numbers of the atypical cells. The mechanism of sickling is unknown. The diagnosis is based on the presence of sickle cells in the blood, anemia and jaundice. No satisfactory treatment has been devised. Survival from an acute attack increases susceptibility to intercurrent disease. Few patients live beyond 35 years of age. BONAR, Salt Lake City.

RECENT OBSERVATION IN SERUM DISEASE. L. W. HUND, J. A. M. A. **99**:909 (Sept. 10) 1932.

Since the establishment of the Durand Hospital nineteen years ago, serum disease has occurred in 28.1 per cent of 2,859 patients who received diphtheria antitoxin,

22.7 per cent of 858 patients who received scarlet fever antitoxin, and 81.8 per cent of 55 patients who received antimeningococcus serum. Serum reactions after diphtheria and scarlet fever antitoxins are determined in part by susceptibility and by the toxic properties of the serum, and to a large extent by the total quantity of serum given. Concentrated diphtheria serums cause about the same reactions as do whole serums of similar bulk. The reactions after scarlet fever antitoxin were slightly less than after diphtheria antitoxin. The appearance of the reactions varied from within a few minutes to within thirty days. Usually they occurred before the eleventh day.

BONAR, Salt Lake City.

HEMOPHILIA. C. L. BUCH, J. A. M. A. **99**:1566 (Nov. 5) 1932.

Thirty-five cases of hemophilia were studied, in twenty-eight of which there was a definite family history. Persons with hemophilia have more daughters than sons, while transmitters have more sons than daughters. Over 71 per cent of the sons of transmitters had hemophilia. Ovarian therapy has produced a good response in nine of nineteen cases and a definite but less marked response in nine. Manifestations of general improvement were an increase in weight, in hemoglobin and in vitality. The specific response consisted in a decrease in the number and severity of the hemorrhages and a lowering of the coagulation time. In vitro, addition of certain ovarian preparations to hemophiliac blood decreases the coagulation time one fourth to one half. The prolonged coagulation time in hemophilia is due to increased resistance of the blood platelets.

BONAR, Salt Lake City.

THE LOCALIZATION AND SPECIFICITY OF CELLULAR SENSITIZATION. HERBERT J. RINKEL and RAY M. BALYEAT, J. Allergy **3**:567 (Sept.) 1932.

The authors believe that specificity of cells is a fundamental consideration in the study of allergy. They report four cases to illustrate the specificity of reactors. Some of the conclusions are as follows:

1. The same exciting factor can produce many forms of allergy depending on the localization of cells specifically sensitive. One or more of these forms may occur in the same patient due to one or several allergens.

2. Skin tests when positive indicate skin sensitivity only. The positive reaction represents one form of allergy, not necessarily related to the others.

3. Sharply circumscribed allergy is best illustrated by cutaneous eruptions. The condition may be limited to definite areas or to certain groups of cells in several locations. This may be due to atopic or contact hypersensitiveness.

4. Skin testing affords no determination of clinical sensitivity; therefore, it should be supplemented in every case by clinical testing.

5. Specific elimination is the therapeutic ideal.

HOYER, Cincinnati.

SKIN TESTS IN 4,589 CASES OF ALLERGIC DISEASE, WITH A CRITICISM CONCERNING ELIMINATION DIETS. GEORGE PINESS and HYMAN MILLER, J. Allergy **4**:18 (Nov.) 1932.

Piness and Miller studied 564,353 individual food protein tests, averaging 104 tests with 17 positive reactions a patient. They conclude that regardless of the heredity, the age of onset, the age when the test was made or the duration of symptoms, 80 per cent of allergic patients should give positive reactions, and that 70 per cent should react positively to foods. Any results lower than this may be traced to promiscuous testing of nonallergic persons, use of unreliable proteins, lack of persistence and completeness in testing, inefficient methods of testing or failure to interpret the reactions properly and to correlate them with the clinical history. From this it may be concluded that elimination diets as a sole reliance for diagnosis or treatment are unnecessary and frequently lead to fallacious conclusions, and that elimination on the basis of skin tests is a rational and reliable point of departure in the treatment of allergic disease.

HOYER, Cincinnati.

AGE INCIDENCE AND CLIMATIC VARIATIONS IN THE MANIFESTATIONS OF SO-CALLED RHEUMATIC FEVER IN WHITE CHILDREN. C. C. MCLEAN, J. Pediat. **2**:320 (March) 1933.

A statistical study was made of the 122 rheumatic children admitted to the Children's Hospital, Birmingham, Ala., from 1922 to 1932. In this city rheumatic fever is largely a disease of the heart. The condition is characterized by an insidious onset, and the cardiac involvement is out of proportion to the severity of the arthritis and chorea. Whereas the incidence of arthritis and chorea was much higher for children in New York City than in Birmingham, the reverse was true for cardiac disease alone. The author concludes that the manifestations of rheumatic fever are more common in the southern states than has previously been recognized.

LEMASTER, Evanston, Ill.

SUBACUTE BACTERIAL ENDOCARDITIS IN A YOUNG CHILD. AMOS U. CHRISTIE and ALFRED HENRY HEALD, J. Pediat. **2**:331 (March) 1933.

A case of subacute bacterial endocarditis in a 5 year old child is reported. At the onset of the illness, the clinical picture was that of acute rheumatic fever. The presence of the *gamma* streptococcus was demonstrated in the blood stream during life.

LEMASTER, Evanston, Ill.

ALLERGIC DISEASES. FRANCIS SCOTT SMYTH, J. Pediat. **2**:349 (March) 1933.

The new developments and trends in allergy of the past few years are briefly reviewed. Special emphasis is placed on passive transfer studies, patch tests, pollen studies on susceptibility to new allergens, bacterial and physical allergy, constitutional studies and therapeutic notes. There are 200 references to recent articles concerning allergy.

LEMASTER, Evanston, Ill.

PYOPNEUMOTHORAX IN INFANTS. L. J. HALPERN and I. PILOT, J. Pediat. **2**:444 (April) 1933.

A case of pyopneumothorax in an infant 6 days old is reported. Septicopyemia caused by Staphylococcus aureus produced a deep abscess of the thigh and subpleural abscesses which ruptured. The roentgenogram was of definite aid in establishing the diagnosis of the pathologic condition of the chest.

LEMASTER, Evanston, Ill.

VULVOVAGINITIS. J. THORNWELL WITHERSPOON and VIRGINIA W. BUTLER, J. Pediat. **2**:463 (April) 1933.

Hospitalization of children with gonorrheal vulvovaginitis is strongly recommended because it affords better facilities for isolation and thorough treatment. The routine management carried out by the authors consists in cleansing the vulva three times a day, followed by vaginal irrigation with a 1:5,000 solution of potassium permanganate and the instillation of 10 cc. of a 5 per cent solution of mercurochrome under pressure. In protracted cases the cervix is painted through a small cystoscope.

LEMASTER, Evanston, Ill.

ERYTHROBLASTIC ANEMIA. J. H. FRIES, E. DUHAN and H. M. SHAIR, J. Pediat. **2**:487 (April) 1933.

Two cases of erythroblastic anemia of Cooley are reported in Greek-American brothers, aged 7 and 3 years. Both boys showed the onset of sallow yellow pallor of the skin when less than 2 years of age, mongoloid facies, "pot-belly" with enlargement of the spleen and the liver, progressive anemia with numerous nucleated red cells and characteristic roentgenologic findings in the bones.

LEMASTER, Evanston, Ill.

BACTERIOLOGIC STUDY OF PYELITIS. PEARL SUMMERFELDT, MARION M. JOHNSTON and MILDRED J. KAAKE, J. Pediat. **2**:493 (April) 1933.

Bacteriologic studies were made on 109 children with pyelitis. All except 5 were girls. Gram-negative bacilli were cultured from the urine far more frequently than were any other organisms. In 40 cases the same species of bacteria were isolated from the stool as from the urine. Agglutinins for the urinary bacteria were demonstrated in the blood serum in 23 cases, but were not present in the blood stream in 25 cases. No definite information could be found to establish the route of infection in pyelitis.

LEMASTER, Evanston, Ill.

CELIAC DISEASE. A. CLEMENT SILVERMAN, New York State J. Med. **32**:1055 (Sept. 15) 1932.

Five cases of celiac disease are reported. Treatment should be started with a diet low in fat and cellulose and with a low buffer content. Skimmed protein milk or skimmed lactic acid milk was used. To this, cottage cheese, egg, scraped beef, sieved liver, gelatin, mashed vegetables and fruit were added later.

AIKMAN, Rochester, N. Y.

CHRONIC NONTUBERCULOUS INFECTION OF THE LUNGS IN CHILDREN. F. H. YOUNG, Brit. M. J. **1**:604 (April 2) 1932.

To the author's mind textbooks are lacking in clear descriptions of nontuberculous pulmonary infections in children. The cases are grouped usually under such names as chronic bronchitis, recurrent bronchitis, unresolved pneumonia, recurrent or interstitial pneumonia and fibrosis of the lung with or without bronchiectasis. Young feels that such a grouping is inexact, though it is likely that the conditions are all different phases or manifestations of a common underlying cause. The physical signs vary widely. Most of the cases occur among children of the poorer classes. Consequently the conditions are neglected, and since the patients seldom die in the hospital autopsies are few. When cases do come to autopsy, however, the disease is so far advanced that it is difficult or impossible to form a clear understanding of the etiologic process. It is in the routine work of clinics for conditions of the chest that these cases are most frequently seen and best studied.

The commonest causes are whooping cough and measles. Lack of painstaking care of these conditions during convalescence will often result in chronic conditions of the chest. An attack of acute bronchitis the initial cause of which is indefinite frequently results in a chronic condition. Rickets undoubtedly plays some part, but its exact etiologic connection is in doubt. Influenza is not so frequently the origin as is commonly thought. Lobar pneumonia and empyema are often given as a common cause. The author thinks this is a mistake. Bronchopneumonia, on the other hand, not infrequently results in a chronic condition. Foreign bodies are emphasized as an etiologic factor. The condition often occurs in families in which there is a tendency to catarrhal inflammation of the chest. Pfeiffer's bacillus is said by some observers to be the most common cause.

The signs and symptoms of the disease are fairly constant. Cough is always prominent; there are often paroxysms, especially on rising in the morning. In the early stages the cough is lost during the summer months, but recurs during the winter; it is eventually present all the year round. Sputum usually is present, and is frequently purulent but not essentially so until the later stages. Streaks of blood are common and occasionally blood in larger amounts is seen. Dyspnea is fairly constant. The health between exacerbations is usually good, but is interrupted by frequent attacks of bronchitis. The weight varies, and an aching pain in the chest is often present. The outstanding feature, however, is the recurrent nature of the attacks. The temperature is frequently irregular, being high during the acute stages; it may be slightly elevated during periods of remission. The child's color is usually good. Early clubbing of the fingers is often found. The physical findings during remission may be surprisingly few.

In the earlier stages the roentgenogram helps very little. It may show increase of striation. The hilar shadows are usually increased. The diaphragm may show some diminution of movement. The heart is often slightly displaced toward the affected side. There is considerable displacement of the heart in the advanced stages. Sometimes cavities are found.

In differential diagnosis, pulmonary tuberculosis is the condition which must be excluded. The roentgenogram and the reaction to the Mantoux test are the positive diagnostic criteria.

The most frequent complication is tuberculosis. The prognosis in cases that are seen early is good.

Careful nursing following measles and whooping cough is the best precautionary measure, with prolonged convalescence in sea air and plenty of sunshine. The author recommends this after attacks of bronchopneumonia or bronchitis. Such treatment when the condition has developed is not so satisfactory. In cases in which it is economically possible, the seaside is recommended. A prolonged rest which does not differ much from that employed in the treatment of tuberculosis is advisable. Further treatment suggested includes the general building up of the patient's vitality and, in certain cases, thoracic surgical intervention.

ROYSTER, University, Va.

A CASE OF MALIGNANT THYMOMA. B. R. NISBET, Brit. M. J. **2**:403 (Aug. 27) 1932.

A case of malignant thymoma is reported. The initial symptoms closely resembled those of laryngeal diphtheria, but they recurred with increasing violence, and several complications set in from which the patient died. The postmortem observations are recorded.

ROYSTER, University, Va.

DIAGNOSIS AND TREATMENT OF GENERALIZED OSTEITIS FIBROSA WITH HYPERPARATHYROIDISM. R. C. ELMSLIE, F. R. FRASER, T. P. DUNHILL, R. M. VICK, C. F. HARRIS and J. A. DAUPHINEE, Brit. J. Surg. **20**:479 (Jan.) 1933.

In this article the complete study of three cases is detailed, including the histories, clinical and roentgen examinations of the bony lesions, chemical investigation, operative treatment and a description of the tumors removed.

The results of the chemical investigation showed a high serum calcium in two of the three patients. In the other patient there was a high normal level. The amount of calcium taken with the food had no effect on the level of the serum calcium.

The serum phosphorus was abnormally low in all three cases. The study of the calcium balance demonstrated the presence of an abnormal calcium metabolism. The study of the phosphorus balance showed a negative balance in only one case, even when the diet was low in calcium and phosphorus. After operation for removal of a parathyroid tumor, the serum calcium fell in all three cases. This level was below normal. The time taken after operation for the low level to be reached varied. The phosphorus of the serum rose after removal of the tumor. The rate of increase was slow, and in only case 3 did it reach a normal level within three months. After operation there was also an increased retention of calcium. The excessive excretion of calcium in the urine disappeared, and excretion was carried out by the intestines. The phosphorus metabolism was little affected after the tumors were removed.

In operating to remove the tumor, one must bear in mind that the position of the parathyroid gland is variable, and that failure to find the tumor may result. Sometimes the tumor is embedded in the thyroid gland.

The diagnosis is based on the presence of generalized osteitis fibrosa with pains and aches in the limbs, spontaneous fractures, cystlike areas of rarefaction in the bones, muscular weakness and wasting. Renal calculi were present in two cases. The relation between the diseases of the bones is not clear, but whether the disease

of the bones is secondary or primary, it would appear that the lesions in the bones will be the immediate cause of the recognition of the condition.

As a result of the removal of the parathyroid tumor, striking improvement in the general health was noted. No further fractures occurred, and considerable density of the bones, especially around the cysts and the cortical bone, was seen from ten to twenty-four months after the operation.

SUMMERFELDT, Toronto, Canada.

AN OUTBREAK OF INFECTIOUS JAUNDICE. G. M. ELLIOTT and C. P. BEATTIE, Edinburgh M. J. **40**:31 (Jan.) 1933.

Elliott reports an outbreak of nineteen cases of this disease in Scotland in the period from September, 1931, to January, 1932. A previous outbreak in 1927 among children was reported in the *Edinburgh Medical Journal* and the data were summarized in the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Fifteen of the nineteen cases occurred in children, who, however, have the disease in a milder form than do adults. The diagnosis consists in demonstrating Leptospira during the first five days of illness by injecting 5 cc. of the patient's blood into the peritoneum of a guinea-pig. The centrifugated urine of the patient after the tenth day of the disease reveals leptospiral organisms, though they are somewhat changed in appearance by acid and bile-containing urine. The centrifugated deposit from the urine may be inoculated into guinea-pigs. This method is not so often successful in revealing the organisms as is the use of the patient's blood, but in this epidemic it was the only method available.

The disease was apparently spread by contact among school children. The chief symptoms present in most cases were vomiting, diarrhea, jaundice and muscular pains. The disease was not fatal. The children's ages were from 5 to 15 years. The treatment was not mentioned.

NEFF, Kansas City, Mo.

INCIDENCE OF PUNCTATE BASOPHILIA. W. T. NELSON, L. LOCKWOOD and K. MCKAY, M. J. Australia **2**:317 (Sept. 10) 1932.

The authors report the incidence of basophilic stippling of the red blood cells in normal persons as compared to that in persons exposed to lead in various occupations. A large number of normal men with no history of contact with lead showed an average of 937 stippled cells per million red cells. As the hazards due to lead increased for persons exposed to it, the number of stippled red cells per million cells increased to as high as 38,000 in cases of clinical lead poisoning. No difference in the appearance of the stippled cells was noted in the blood smears between normal persons and persons suffering from lead poisoning.

GONCE, Madison, Wis.

BRIGHT'S DISEASE: ITS CLASSIFICATION. G. T. JAMES, M. J. Australia **2**:321 (Sept. 10) 1932.

The author discusses the present confusing classification of nephritis and the limitation of knowledge of the disease. He offers a simpler classification based on the pathologic changes of the organ in disease as follows: (1) the inflammatory or glomerulonephritic group, (2) the degenerative or nephrotic group and (3) the arteriosclerotic or nephrosclerotic group.

GONCE, Madison, Wis.

TWO CASES OF LIVER ABSCESS. D. B. WALKER, M. J. Australia **2**:632 (Nov. 19) 1932.

The author reports two cases of abscess of the liver which developed as a complication of acute catarrhal jaundice.

GONCE, Madison, Wis.

EXOPHTHALMIC GOITRE IN A GIRL AGED TWO YEARS. E. H. M. STEPHEN, M. J. Australia **1**:29 (Jan. 7) 1933.

The author reports a case of exophthalmic goiter occurring in a 2 year old child.

GONCE, Madison, Wis.

MALIGNANT LYMPHOGRANULOMATOSIS COMPLICATING THREE CASES OF TUBERCULOSIS IN CHILDHOOD. P. NOBÉCOURT, RENÉ MARTIN and R. LIÈGE, Arch. de méd. d. enf. **36**:73 (Feb.) 1933.

Continuing an investigation which has already been signalized by several valuable contributions on the clinical and pathologic aspects of three cases, the relation between malignant lymphogranulomatosis and tuberculosis is considered. All three children, aged 9, 6 and 5 years, respectively, presented cervical adenitis. The glands were examined through biopsy, and in no case could the lesions or the bacilli of tuberculosis be demonstrated. Inoculation of animals also gave entirely negative results. It was inferred from these facts that tuberculosis per se was not responsible for the granulomatous invasion.

It was likewise found in one of the cases with extreme involvement of the spleen that the characteristic histologic picture of tuberculosis was absent in this organ. A further item in this intensive research was the continuous and total negativity of the cutireaction, which could be interpreted as being due to either the particular modality of the tuberculosis or an anergistic action of the coincident lymphogranulomatosis.

The authors conclude that the latter may be considered as an independent condition prone to keep in abeyance the well known phenomena which one usually depends on for the diagnosis of tuberculosis in the young.

AMESSE, Denver.

CHRONIC DIARRHEA WITH EDEMA AND OLIGURIA IN AN INFANT. RENÉ MATHIEU, Bull. Soc. de pédiat. de Paris **30**:460 (July 12) 1932.

A boy, aged 9 months, had loose stools since birth, and showed edema and oliguria, which were more marked on some occasions than on others. He was considered to have an intolerance for milk, or anaphylaxis, but the author believes that his condition was due to a metabolic disturbance in the exchange of water and salt in the body. Dietary treatment was of no avail, but the administration of diuretics, notably theobromine, and the exhibition of thyroid extract gave good results; the diarrhea ceased, the edema disappeared, the urinary output became normal in amount, and the general condition was excellent. This infant furnishes an example of the syndrome of hydrolability of Finkelstein, which is called dysosmosis by Lesage.

BENJAMIN, Montreal, Canada.

MEGADOLICHOCOLON WITH ARREST OF DEVELOPMENT IN A CHILD THREE YEARS OLD (CELIAC DISEASE?). GIRAUD and ASTIER, Bull. Soc. de pédiat. de Paris **30**:468 (July 12) 1932.

A boy was apparently well until 6 months of age, when he began to suffer from persistent diarrhea. When first seen, at 2½ years of age, he was markedly emaciated and short, and had a prominent abdomen. There was never any vomiting or abdominal pain. He had an occasional slight fever. Roentgenologic examination showed an enormously dilated colon, which was also longer than normal. It took 2 liters of barium-containing fluid to fill the large bowel. He had no period of constipation, although the latter is the rule in cases of megacolon. Dietary treatment had little effect. Two courses of ultraviolet irradiation, as well as a period of antisyphilitic treatment, were followed by marked improvement. There was no evidence of hereditary syphilis. There are points of striking resemblance to celiac disease in this case, but the digestive disturbance is regarded as secondary to the intestinal malformation.

BENJAMIN, Montreal, Canada.

ALLERGY IN INFANTS. P. WORINGER, Nourrisson **20**:324 (Nov.) 1932.

Allergy and eczema in infants are closely related. The degree of allergy can often be determined by testing with intracutaneous injections of the diluted albumin of an egg. In infants who are constitutionally allergic a sufficiently large dose of the allergen will give, in addition to the positive cutaneous reaction, a generalized urticaria or even symptoms of anaphylactic shock. The serum of these persons will give a positive reaction to the Prausnitz-Küstner transfer test. Occasionally generalized reactions occur in infants with a negative cutaneous reaction. Other infants have a positive cutaneous reaction alone. The serum of the latter always gives a negative reaction to the transfer test, and the eczema is less severe and less prolonged.

McCLELLAND, Cleveland.

BENIGN CONDENSING OSTEITIS. J. ISERBYT, Rev. d'orthop. **20**:148, (March-April) 1933.

Iserbyt reports a case of benign condensing osteitis in a woman, aged 28. From the age of 23, the patient complained of swelling in the left leg accompanied by pain; these symptoms were relieved by rest. Physical examination showed nothing of consequence except the condition of the left leg; the swelling extended from the ankle to the midregion of the calf. Pressure over the tibia caused pain, especially at the level of the epiphyses. Pressure over the muscles in the calf also produced pain. The contour of the tibia appeared normal, and there was no limitation of motion in any of the joints of the limb. The Wassermann test was negative. Roentgenograms showed a lineal condensed area in the lower and upper ends of the tibia and in the lower end of the femur. No other sites of condensation were found.

Antisyphilitic treatment gave no relief, nor was the condition influenced by any other form of therapy.

The localization of the lesions was atypical.

RYAN, Vancouver, Canada.

RECKLINGHAUSEN'S DISEASE. CHARLES PARISEL, Scalpel **85**:810 (July 2) 1932.

A girl 10 years of age with osteitis fibrosa generalisata had multiple spontaneous fractures of both femurs, cystic formations in most of the long bones and rarefaction of the cortical tissue. The blood calcium rose to 12.6 mg. per hundred cubic centimeters, and calcariuria increased. No tumor could be felt in the skin. The author proposed to explore the area involved for a parathyroid adenoma.

VINTON, Brooklyn.

SYNDROME OF HAND-SCHÜLLER-CHRISTIAN. M. PINCHERLE, Arch. ital. di pediat. **1**:1 (Sept.) 1932.

A carefully studied case of a girl, aged 4 years, is presented in great detail. The outstanding features were the characteristic defects of the frontal, parietal, temporal and occipital bones and of the left ilium and scapula, together with exophthalmos, precocious eruption of the secondary teeth, polyuria, increased blood cholesterol (254 mg. per hundred cubic centimeters), and general maldevelopment. The diagnosis was established by biopsy of a lesion of the parietal bone. The child was followed up for two years, during which time there was almost complete retrogression of the lesions of the bone with pronounced improvement of the general condition.

Professor Pincherle (University of Bologna) also gives a review of this syndrome, including an analysis of a bibliography of more than 100 titles. His scholarly paper cannot be presented in abstract, but should be read by all who have a particular interest in this subject.

DOOLEY, Kent, Conn.

CHANGES OF THE BONES IN LEAD POISONING AND IN SO-CALLED MENINGITIS IN INFANTS. M. KASAHARA, H. HIROSHIMA and T. TOKUYAMA, J. Pediat. (Tokio), no. 391, Dec. 20, 1932, p. 2288.

The authors made roentgenologic examinations of seventy-eight cases of lead poisoning and of so-called meningitis due to lead in infants. The shadows from lead in the various bones are recorded in table 1.

Chemical analysis of the long bones demonstrated a greater amount of lead in the metaphysis than in the diaphysis (table 2).

TABLE 1.—*Results of Roentgenographic Examination of Bones in Lead Poisoning*

Bone Region	Number of Examinations	Number of Positive Shadows
Lower end of femur	77	77
Upper end of tibia	77	77
Lower end of tibia	76	76
Lower end of fibula	74	74
Upper end of fibula	77	76
Lower end of radius	78	77
Lower end of ulna	78	77
Bones of foot	74	68
Ilium	60	55
Upper end of humerus	58	52
Lower end of humerus	78	67
Upper end of femur	78	48
Upper end of radius	78	63
Anterior end of ribs	71	55
Bones of the hand	71	55
Metatarsal nucleus	76	56
Scapula	69	39
Sternal nucleus	76	41
Upper end of ulna	78	39
Epiphyseal nucleus	78	33
Metacarpal nucleus	73	30

TABLE 2.—*Results of Chemical Analysis of Long Bones in Lead Poisoning*

Case	Amount of Lead at Metaphysis, Mg. per 100 Gm.	Amount of Lead at Diaphysis, Mg. per 100 Gm.
1	13.09	5.30
2	17.69	9.64
3	34.70	22.42
4	23.48	30.41

It was found, however, that the ends of the bones shown by actual chemical test to contain large amounts of lead did not throw correspondingly heavy shadows on the roentgenograms. Thus, the authors were led to conclude that the heavy lines on the roentgenograms in cases of lead poisoning are not necessarily due to the presence of lead but to increased density due to hypercalcification.

KATO, Chicago.

Nervous Diseases

MENINGOCOCCIC MENINGITIS AND EPIDEMIC MENINGO-ENCEPHALOPATHY: REPORTS OF ONE HUNDRED AND TWENTY-TWO ADDITIONAL CASES IN THE INDIANAPOLIS EPIDEMIC AND OF SIXTY-EIGHT CASES OF AN EPIDEMIC MENINGO-ENCEPHALOPATHY. G. E. KEMPF, L. H. GILMAN and L. G. ZERFAS, Arch. Neurol. & Psychiat. **29**:433 (March) 1933.

Sixty-eight cases of meningitis differing from any of the clinical types previously described are reported from Indianapolis. In some cases the onset was slow, requiring a week or more; in others it was fulminating. A gram-positive organism was isolated. Antimeningococcic serum was of no value in treatment.

The microscopic changes in the brain resembled those of toxic encephalitis. This group of cases paralleled and followed an epidemic of meningococcic meningitis, but the symptoms were decidedly different.

BEVERLY, Chicago.

INFLUENCE OF VARIATIONS IN FLUID INTAKE ON INTRACRANIAL PRESSURE IN "EPILEPTICS." FRANK FREMONT-SMITH and H. HOUSTON MERRITT, Arch. Neurol. & Psychiat. **29**:454 (March) 1933.

The authors studied the effect of the intake of fluid on cerebrospinal fluid pressure and on convulsions. They found that the ingestion of from 1 to 2 liters of water causes no appreciable change in the cerebrospinal fluid pressure in patients suffering from convulsions, provided diuresis is normal. The restriction of fluids tends to diminish the number of convulsions, and the increasing level of the intake of fluid may increase the number of seizures.

BEVERLY, Chicago.

ACALCULIA (HENSCHEN): A CLINICAL STUDY. H. DOUGLAS SINGER and ABRAHAM A. LOW, Arch. Neurol. & Psychiat. **29**:467 (March) 1933.

Acalculia is a special defect in the ability to do arithmetic. The authors describe a case in a patient who had carbon monoxide poisoning.

BEVERLY, Chicago.

MÉNIÈRE'S DISEASE: DIAGNOSIS AND TREATMENT. C. C. COLEMAN and J. G. LYERLY, Arch. Neurol. & Psychiat. **29**:522 (March) 1933.

The authors report excellent results in the treatment of eight patients with Ménière's disease by intracranial section of the eighth nerve.

BEVERLY, Chicago.

PNEUMORACHIOCLYSIS AND CERVICOLUMBAR IRRIGATION IN THE TREATMENT OF MENINGOCOCCIC MENINGITIS. LEON HASTINGS CORNWALL, Arch. Neurol. & Psychiat. **29**:619 (March) 1933.

Pneumorachioclysis consists in the intrathecal injection of small amounts of air into the lumbar region followed by cervical lumbar irrigation. It is found to be especially valuable in cases of meningitis to break up adhesions which form after the injection of serum into the spinal canal.

BEVERLY, Chicago.

AN ATTEMPT TO TRANSMIT POLIOMYELITIS TO SPLENECTOMIZED GUINEA-PIGS. HERMAN CHOR, Arch. Path. **15**:387 (March) 1933.

Splenectomized guinea-pigs did not acquire the nerve lesions characteristic of poliomyelitis following inoculation with potent monkey virus, either in direct or in passage experiments. However, the splenectomized guinea-pigs showed a decrease in resistance to such inoculation, as was evidenced by fever, general sluggishness and lymphoid hyperplasia, with death often occurring within fourteen days.

LEMASTER, Evanston, Ill.

ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS. MAURICE BRODIE, J. Exper. Med. **56**:493 (Oct.) 1932.

Working with monkeys, the author was able to produce immunity actively by a single injection of a subinfective dose of the virus of poliomyelitis obtained from the spinal cord of animals suffering from the disease. Larger doses induced the disease in unprotected animals, but by the antecedent, simultaneous or subsequent (after three days) injection of either immune human or immune monkey serum he was able to prevent the appearance of paralysis in animals thus inoculated. The animals later showed varying degrees of immunity. When an excess of the immune serum was given, the degree of immunity which developed was con-

siderably less than when smaller but sufficient doses were given. By standardizing the poliomyelitis virus used, Brodie was able to measure the protective strength of the convalescent serums of monkeys and human beings. LUECKE, Dallas.

A COMPARISON BETWEEN CONVALESCENT SERUM AND NONCONVALESCENT SERUM IN POLIOMYELITIS. MAURICE BRODIE, J. Exper. Med. **56**:507 (Oct.) 1932.

By injecting into monkeys measured amounts of a standardized poliomyelitis virus and varying amounts of human serum from persons who had had the disease and from those who had not had it, the author was able to determine the relative protective value of serum from these two sources. In this study the subjects, all of whom were normal urban adults, were divided into three classes: (1) those who had never had the disease and gave no history of ever having come in contact with any one who had it, (2) those who had never had the disease but had been in contact with one or more who had it and (3) those who had had the disease. Of serums from twenty-nine so-called normal urban adults, seven had less than two-fifths, three had two-fifths, two had three-fifths, eight had four-fifths and nine had the full neutralizing power of the average of five batches of pooled convalescent serum. Serums from known contacts and those from avowed noncontacts were equally represented in the serums of low potency, but in the serums of higher potency those from the known contacts were predominantly represented. The pooled serums of known contacts and those of noncontacts were, respectively, a little above and a little below half the strength of the pooled convalescent serum. Of the serums from two series of patients with early stages of poliomyelitis, one treated with normal serum of proved protective power and the other with convalescent serum, neither showed any advantage over the other.

LUECKE, Dallas, Texas.

MENINGOCOCCUS MENINGITIS. STANLEY S. LAMM, J. Pediat. **2**:273 (March) 1933.

The principles and methods employed by the author in the treatment of epidemic meningitis are discussed. From 1924 to 1931, there were fifty-three infants and children treated for meningitis, with a total mortality of 30 per cent. The criteria adopted to determine when serum therapy should be discontinued consisted of two successively negative cultures of the spinal fluid, return of the sugar in the spinal fluid to normal, reduction of the total number of white cells in the blood and spinal fluid to normal and improvement in the clinical appearance of the patient. When spinal fluid drained poorly through the needle, injections of small amounts of air increased the flow. When the posterior basic type of meningitis was suspected, serum was introduced intracisternally from the onset. A few illustrative cases are cited. LEMASTER, Evanston, Ill.

POLIOMYELITIS: REPORT OF SIMULTANEOUS CASES IN ONE FAMILY. WALTER B. STEWART, J. Pediat. **2**:393 (April) 1933.

Three members of a family had poliomyelitis, two with paralysis and one without paralysis. A fourth person in the family had poliomyelitis of an abortive type, and a fifth member had a simultaneous infection the nature of which was not determined, but which also may have been poliomyelitis of an abortive type. The father was a physician and had been in contact with poliomyelitis.

LEMASTER, Evanston, Ill.

USE OF EPHEDRINE IN THE TREATMENT OF NARCOLEPSY IN CHILDREN. A. WILMOT JACOBSEN, J. Pediat. **2**:414 (April) 1933.

Narcolepsy is a term coined by Gelineau in 1880 to describe a clinical condition characterized by frequently recurring attacks of sleep without apparent cause, associated with curious attacks of temporary loss of tone in the voluntary muscles

precipitated by emotion. Although in a few cases a definite cerebral organic change has been found, in the majority no definite etiologic factor has been demonstrated. The author reports narcolepsy in three children, one 13 and two 9 years of age. Immediate symptomatic recovery from the tendency to frequent and prolonged sleep was obtained by the use of ephedrine sulphate given by mouth.

LeMaster, Evanston, Ill.

Training the High Grade Mental Defective for Community Life. Sanger Brown, Jr., Ment. Hyg. **16**:440 (July) 1932.

For the purposes of the article, Brown defines high grade mentally defective persons as borderline types and morons whose intelligence quotients fall into the range between 65 and 79. These children on parole often fail seriously in their efforts to make social adjustment, in spite of what appears to be excellent institutional training. The first cause for the failure is the poverty of opportunity for social training which is inevitably the lot of a child surrounded by mentally defective children. This points the way to a method for remedying the fault, namely, intelligent social training. Mentally defective children of the higher grade should be housed in separate quarters; infants should be placed in a well equipped and intelligently manned nursery school, while somewhat older children should attend an institutional kindergarten. The older children should be housed in cottages under the supervision of trained nurses. They should be sent to the regular community schools, away from the grounds of the institution. It may be necessary to modify the curriculum or even to provide separate classes, but the school building they use should be part of the community's public school system, and not part of the general training school for the feebleminded. When possible, boarding homes under general institutional supervision should be established, so that these children may live in the atmosphere of a home and take part in the church, school, recreational and other social activities of the ordinary community routine. Only in this manner will it be possible to overcome the serious limitations inherent in institutional life as a training for social responsibilities.

Davidson, Newark, N. J. [Arch. Neurol. & Psychiat.]

The Walter E. Fernald Plan for the Examination of Retarded School Children. Neil A. Dayton, New England J. Med. **207**:913 (Nov. 24) 1932.

The Fernald plan comprises the following factors:

1. There is a traveling clinic which visits each school.

2. The personnel consists of a psychiatrist, a psychologist and a social worker. In addition, the school provides a school teacher, a school nurse and a visiting teacher, who assist in certain phases of the examination.

3. The ten-point scale examination includes: the family history, the personal and developmental history, the history of the progress in school, the social history, the personal characteristics and social conduct, economic efficiency, practical knowledge, the school work, physical examination and psychologic tests.

4. The method of procedure is as follows: All retarded children are listed by the school superintendent, and the list is sent to the psychiatrist of the clinic. A date is set for the visit of the clinic, and the history and test forms are forwarded to the superintendent. The histories are completed by a social worker, a school nurse or a visiting teacher. The school tests are completed by an assigned teacher. The traveling clinic then visits the school (a quiet section of the school is highly desirable for the conducting of the tests), and the examination is completed by the staff of the clinic, at an average rate of six examinations per day. The summary and diagnosis are reported by the psychiatrist, who later interviews the parents. At the conclusion of the examination, a complete report is made to the superintendent, giving the facts in reference to the data reported from the examination. The psychiatrist then offers recommendations in regard to educational, social and physical problems.

In approximately 50 per cent of the cases the educational advice is "place in a special class." Approximately 4 per cent of the children are recommended for admission to a state school for mental defectives. In other cases the problem is solved by placing the child in a grade to suit his mental age. In regard to social problems, the urgent need at present is for more complete social supervision of retarded children. Physical examinations of retarded school children show an unusual number of defects. Sixty-five per cent of these children are advised to consult a physician or a dentist immediately.

5. The average intelligence quotient of the 20,473 retarded children who were examined between 1921 and 1930, inclusive, was 71.7.

6. Since the inauguration of the school clinic system in 1914, 51,205 examinations of retarded children have been conducted. Approximately 41,000 of this number are first examinations, and 10,000 are reexaminations.

GENGENBACH, Denver.

PERSONALITY AND CATATONIC DEMENTIA PRAECOX. JOSEPH R. BLALOCK, Psychiat. Quart. **6**:625 (Oct.) 1932.

Blalock studied the personalities of twenty-five men suffering from catatonic dementia praecox and free from physical disease. The Hoch-Amsden technic for studying personality, as modified by Kirby, was used. Nine of the patients were definitely introverted, and one was definitely extroverted; the remaining fifteen were well balanced in this field. There was nothing striking in the analysis of the traits as to knowledge, intelligence or judgment. The majority were awkward in the use of tools. The output of energy was definitely but not markedly reduced. Three fourths of the patients had always been bashful, and two thirds of them were stubborn, aloof, sensitive and devoid of extensive external interests. Nearly all of them were overconscientious, diligent, undemonstrative, relatively friendless, truthful and strongly attached to their mothers. Most of them seemed unimaginative, matter-of-fact and logical and orderly in their type of thinking. They were placid, phlegmatic and even-tempered and showed little tendency to brood. Sexual adaptability appeared to be defective in most of the patients. Modesty and prudishness were found in excess. These patients were inclined to be shy in the presence of girls and secretive on the subject of sex. Feelings of inferiority were present, but not to an unusual degree.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

CONDITIONED REFLEXES AND HABIT FORMATION. W. HORSLEY GANTT, Brit. M. J. **1**:517 (March 19) 1932.

A description of habits is given with an explanation of both conditioned and unconditioned reflexes. The teaching of Pavlov is closely followed and often quoted. There follow a description and explanation of both indirect and direct inhibitions, as well as of associative inhibitions. A brief discussion is then given of the relation between the various inhibitions and conditioned reflexes and of the formation of habit. The author explains the application of such observations to the development of morals and the formation of prejudices, and finally discusses how the interaction of all these stimuli and influences relates to behavior.

ROYSTER, University, Va.

FULMINATING MENINGOCOCCAL MENINGITIS WITH RECOVERY. J. N. C. FORD, GEOFFREY SHERA and JAMES PURVES-STEWART, Brit. M. J. **1**:558 (March 26) 1932.

The authors report a case of fulminant meningococcic meningitis in which the patient was treated intensively by cisternal puncture and lumbar puncture. The case was complicated by multiple arthritis, with pus in the knees. The patient ultimately recovered.

ROYSTER, University, Va.

CONGENITAL TERATOID NEUROBLASTOMA OF THE BRAIN. K. C. CHANDHURI, J. Indian M. A. **2**:141 (Dec.) 1932.

A congenital tumor of the brain of an infant is described. The tumor was a neuroblastoma with cartilage and bone formation, that is, a teratoid tumor with one-sided and marked development of the nerve elements only. Its point of origin was perhaps the third ventricle, without, however, any relation to the hypophysis.

AUTHOR'S ABSTRACT.

JUVENILE TYPE OF DIFFUSE FAMILIAL CEREBRAL SCLEROSIS. D. DUTHOIT and L. VAN BOGAERT, Arch. de méd. d. enf. **36**:137 (March) 1933.

References are made in the literature, not only under the designation of diffuse familial cerebral sclerosis, but under such names as diffuse periaxial encephalitis, to an obscure disorder commonly known as Heubner-Schilder's disease. It is essentially paraplegia, which develops later into quadriplegia and terminates in the complete loss of motor functions. With the widespread paralysis there is associated an involution of the higher psychic functions, resulting sooner or later in dementia. From an anatomic point of view the disease may be described as an inflammation of the white substance the evolution of which is in the direction of sclerosis.

The authors discuss the proper classification of the disease and its symptomatology and physiopathology, and report at length their clinical observation in two cases.

AMESSE, Denver.

ENCEPHALITIS IN CHILDREN AND POLIOMYELITIS. ROBERT DEBRÉ, ROBERT BROCA and JULIEN MARIE, Bull. Soc. de pédiat. de Paris **30**:224 (April 19) 1932.

A boy, aged 13½ months, had acute encephalitis. The possibility of the poliomyelitic virus being responsible for the production of encephalitis is discussed. The authors believe that encephalitis and poliomyelitis have separate and distinct etiologic viruses. In this case the neutralizing test for the poliomyelitic virus gave negative results. A positive reaction to the neutralizing test does not necessarily prove that the etiologic virus is that of poliomyelitis, since serum from persons who have no history of poliomyelitis, as well as serum from some patients who have had encephalitis, has been shown to contain substances which neutralize the virus.

BENJAMIN, Montreal, Canada.

PERSISTENT TRAUMATIC SUPRA-ORBITAL NEURALGIA CURED BY IONIZATION WITH NITRATE OF ACONITINE. P. DUHEM and M. FÈVRE, Bull. Soc. de pédiat. de Paris **30**:246 (April 19) 1932.

A girl, 11 years old, had suffered from a penetrating wound of the left supra-orbital region four years previous to treatment. She had experienced almost continual severe pain about the left eye and could hardly see because of it. Thirteen treatments by means of a 1:4,000 solution of nitrate of aconitine placed about the positive pole, which rested on the painful area, while the negative electrode was applied to the nape of the neck, were given. Each treatment lasted half an hour; a current of from 5 to 6 ma. was employed. The length of the interval between treatments is not mentioned. The child was completely cured.

BENJAMIN, Montreal, Canada.

MENINGEAL FORM OF EPIDEMIC POLIOMYELITIS. L. LARUELLE, Scalpel **85**: 1201 (Sept. 24) 1932.

The reappearance of poliomyelitis in Belgium in July and August, 1932, was marked by the frequent occurrence of meningeal forms. The cases under consideration form a transitional series between a purely meningeal type and the

classic type. The author describes several forms: a purely meningeal form, a meningoparalytic form and an ascending form (Landry's type). The differential diagnosis between cerebrospinal meningitis and tuberculous meningitis should be made at the outset. The author reviews the various points of differential diagnosis and emphasizes the importance of disturbances of the tendon reflexes, particularly Kernig's sign, and the early appearance of paralytic symptoms. On examination the cerebrospinal fluid shows an early but temporary polynucleosis, followed by lymphocytosis and the appearance of mesodermal cells. There is feeble hyperalbuminosis. Hyperglycorrhachia is less pronounced than in tuberculous meningitis.

VINTON, Brooklyn.

PERIOSTEAL ZYGOMATIC REFLEX. JOHANN SUSMANN GALANT, Kinderärztl. Praxis **3**:453 (Oct.) 1932.

The author describes a new periosteal reflex obtained by tapping the zygoma. A positive reaction is similar to the Chvostek phenomenon, but it does not have the same significance. Unlike the Chvostek sign, it is never obtained in normal persons and often indicates severe organic nervous disease, such as progressive paralysis and chronic alcoholism. Pediatricians are advised to study this reflex in infants to discover its exact meaning.

HUENEKENS, Minneapolis.

TREATMENT OF CHOREA MINOR WITH BIER'S HYPEREMIA. PAUL ESAU, Kinderärztl. Praxis **3**:492 (Nov.) 1932.

The use of Bier's hyperemia in the treatment of chorea has been known for thirty years and has been described in the literature during the past ten years, but the method is still comparatively unknown to the pediatrician. A woven rubber bandage with hooks and eyes is wrapped around the neck and is gradually tightened to produce the desired hyperemia. On the first day it is allowed to remain for from three to four hours, on the second day for ten hours and thereafter for twenty-two hours, with a two hour period of rest. The author praises the method as the most effective treatment yet devised; in comparison to phenyl-ethyl-hydantoin, it has a more favorable effect and is less dangerous. Its action depends partly on the increase of fluid in the cranium, resulting in a mild increase in intracranial pressure, and, above all, on the increase of carbon dioxide in the passively congested blood.

HUENEKENS, Minneapolis.

PRODROMAL SYMPTOMS, ABORTIVE FORMS, PROPHYLAXIS AND TREATMENT OF POLIOMYELITIS. LEO LANGSTEIN, Kinderärztl. Praxis **3**:537 (Dec.) 1932.

This article is based on a study of 1,000 cases of poliomyelitis. The most important prodromal symptoms are severe pain in the extremities, back and abdomen; muscular weakness, demonstrated by passive motion and resistance, and, finally, meningismus. The diagnosis of the abortive forms is uncertain, since the specific cause of poliomyelitis is not known. Langstein urges German physicians to use convalescent serum more freely as a prophylactic and to administer it in the prodromal stages; he quotes Pfaundler to emphasize the fact that it can do no harm and may do good, even in the paralytic stage. There is no proof that convalescent serum is effective at any stage, but in the absence of other therapeutic agents it deserves a thorough trial.

HUENEKENS, Minneapolis.

OUR EXPERIENCE WITH AN EPIDEMIC OF POLIOMYELITIS. O. TEYSCL, Časop. lék. česk. **70**:1796 (Dec. 18) 1931.

The author reports a series of seventy-four cases of anterior poliomyelitis, thirty-six of which had no ultimate residue. In some cases it was difficult to differentiate the condition from basal meningitis. Seven of the cases were ultimately diagnosed as polioencephalitis. Petitte's serum, convalescent serum, the roentgenotherapy of Bordier and spinal injections of 40 per cent methenamine were used, with no

apparent improvement. The author holds that poor therapeutic results are due to the affinity of the virus and the tissues involved. He feels that convalescent serum has the best possibilities.

STULIK, Chicago.

Diseases of the Eye

EXOPHTHALMOS: ITS OCULAR SYMPTOMS. HAROLD H. JOY, New York State J. Med. **33**:68 (Jan. 15) 1933.

Bilateral exophthalmos may be caused by: (1) infantile scurvy, which may produce periosteal orbital hemorrhage and exophthalmos; it is sudden in onset, causes ecchymosis or edema of the lids and yields readily to antiscorbutic treatment; (2) Christian's syndrome, characterized by exophthalmos with large defects in the skull bones, especially about the orbit; visual symptoms may occur; (3) chloroma, which may cause edema of the lids and exophthalmos; the parotid and other glands may be swollen; panophthalmitis may occur; (4) oxycephaly or tower skull; (5) hydrocephalus or rickets, in which it has little diagnostic importance.

AIKMAN, Rochester, N. Y.

TRANSMISSION OF TRACHOMA TO EUROPEAN CHILDREN IN INFECTED REGIONS. F. MOTAIS, Rev. internat. du trachome **9**:30 (Jan.) 1932.

Trachomatous infection generally occurs in infancy, and then from contamination by those infected—usually the mother or the nurse. Europeans should be warned that their children, when taken care of by native domestics, are exposed to this danger.

J. E. LEBENSOHN. [ARCH. OPHTH.]

THE "WILD GLANCE" OF SUCKLINGS. B. EPSTEIN, Med. Klin. **29**:1010 (July 21) 1933.

Epstein describes a symptom of the eyelid corresponding to Dalrymple's sign or von Graefe's sign occurring in neuropathic infants. Because the sign gives the infant a disturbed, alarmed expression, he terms it *wilde Blick*. In general, this symptom was temporary and fluctuated in intensity, being most severe when the patient showed nervous alterations or marked disturbance of the general condition. It was often noted at the onset of alimentary toxicosis. Three good photographs illustrate the description.

DOOLEY, Kent, Conn.

DESTRUCTION OF BLOOD VESSELS IN JUVENILE GLAUCOMA. B. G. TOWBIN and L. I. WILENSKI, Ztschr. f. Augenh. **80**:141 (April) 1933.

Glaucoma in young persons occurs in two forms: (1) that in which the size of the globe increases, hydrophthalmos, and (2) that which clinically resembles the glaucoma of older persons, or juvenile glaucoma. During a period of ten years there were observed in the ophthalmic clinic of the I. Moscow State University 784 cases of glaucoma, the disease occurring in 12 persons not over 30 years of age. In the ophthalmic clinic of the Kasan State Institute, among 256 cases of glaucoma there were 14 in which the patient was under 30 years of age—5 with hydrophthalmos and 9 with juvenile glaucoma. The authors believe that every patient with juvenile glaucoma should have a careful general examination, for departures from the normal may be found which may prove significant from the standpoint of causation. They cite their findings in an extensive examination of one patient with juvenile glaucoma who showed changes in the vascular system. 1. The capillaries of the skin at the bed of the finger-nails were examined with the Leitz capillaroscope. Changes were observed in the capillary network: narrowing of the arterial branches, stasis, dilatation of the venous branches and corkscrew vessels. 2. There was a moderate increase in the blood pressure. 3. There were changes in the concentration and secretion of the urine.

H. L. BEGLE. [ARCH. OPHTH.]

THE FAMILIAL APPEARANCE OF ECTOPIA LENTIS. PAVLA KREDBOVA, Časop. lék. česk. **71**:871 (July 8) 1932.

The author presents the family sequence during four generations in which seventeen members had either unilateral or bilateral ectopia lentis, either with or without myopia or coloboma. There were three in the first, three in the second, eight in the third and, to date, three in the fourth generation. Consanguinity is regarded by some as a factor. The question of dominant and recessive factors in heredity is discussed. This report points to ectopia lentis as a dominant hereditary factor.

STULIK, Chicago.

Diseases of the Ear, Nose and Throat

THE RELATION OF EXOPHTHALMOS TO NASAL SINUS DISEASE. RAYMOND W. HAWKINS, New York State J. Med. **33**:65 (Jan. 15) 1933.

Four types of pathologic process in the nasal sinuses may produce exophthalmos: (1) acute or chronic infections in the frontal sinus or in one of the ethmoid cells; (2) cavernous sinus thrombosis of nasal origin; (3) benign tumors, usually mucocele or osteoma; (4) malignant disease of the ethmoid bone.

Suppuration of the ethmoid sinuses is the most common cause of inflammation of the orbit in children. In adults, the frontal sinuses are more often involved.

Two cases are reported. In one, a boy, aged 14 years, had left frontal headache and protrusion of the left eye following a cold in the head and profuse purulent discharge from the left nostril. Both the left frontal sinus and the antrum were involved. After careful irrigations the exophthalmos began to subside, and the boy recovered in ten days.

In the other, a boy of 13 years had pain over the right eye for four days before admission; later the lids became swollen and edematous, and the next day exophthalmos developed. He had severe right frontal headache and a temperature of 103 F. The exophthalmos was marked. The right maxillary, ethmoid and frontal sinuses were involved. The right frontal sinus and the anterior ethmoid cells were opened externally. Many complications developed, including cellulitis of the scalp and osteomyelitis of the frontal and parietal bones. The exophthalmos disappeared. Later, an extradural abscess was found and drained. The child recovered.

AIKMAN, Rochester, N. Y.

A RARE MALFORMATION OF THE PETROUS BONE. E. G. MAYER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:226 (July 14) 1933.

The case reported by Mayer was observed during the roentgenologic examination of the skull of a 19 year old patient because of a suspected tumor of the cerebellopontile angle. The malformation was limited to the labyrinth of the left side and involved chiefly the vestibular portion. The diameter of the internal acoustic meatus on the left side was about one-half that of the right side, and the vestibule was malformed. The lateral semicircular canal on this side was shorter and its lumen larger than that of the right side. In place of the superior and posterior semicircular canals there was only one semicircular canal located in the sagittal plane of the skull. The atypical location of this semicircular canal can be explained by its embryonic development. The superior and posterior semicircular canals develop in the auditory vesicle from a common fold, which is originally in the sagittal plane of the skull. The development of the two semicircular canals from this fold occurs at a late period. The fact that the atypical semicircular canal was unusually small toward the back suggests that the malformation affected the anlage of the posterior semicircular canal the most. There was no roentgenologic indication of an endocranial space-limiting process. While this does not exclude the existence of a tumor, it is at least very unlikely that the

unusual constriction of the internal acoustic meatus was caused by a tumor of the cerebellopontile angle. It was probably due to the existing malformation.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ROENTGENOTHERAPY OF TONSILLITIS. E. HASENJÄGER, Med. Klin. **29**:1311 (Sept. 22) 1933.

Since 1929, Hasenjäger has treated forty-seven patients with subacute and chronic tonsillitis by means of roentgen rays. In those cases which show a moderate amount of inflammation, he uses a dosage of from 20 to 25 per cent of a unit skin dose, and in more chronic cases, as much as 40 per cent. Most of his patients were treated only once, although several were treated two or three times at intervals of from four to six weeks. Of thirty-two cases which he was able to follow up, he believes that there was a cure in twenty-three, improvement in five and no improvement in four. Half the patients were children between the ages of 4 and 15 years. Roentgenotherapy can be used in all cases in which surgical intervention is contraindicated, save perhaps in children under the age of 2 years.

Hasenjäger also treated fifteen patients with acute tonsillitis, with lymphadenitis or with peritonsillitis, and seemed to get satisfactory results. The danger of increased swelling and possible edema of the glottis seems slight even in the treatment of patients with very severe cases, unless edema of the glottis is already present.

DOOLEY, Kent, Conn.

INFLAMMATORY COMPLICATIONS OF THE WOUND FOLLOWING TONSILLECTOMY. N. SIEGMANN, Monatschr. f. Ohrenh. **66**:1458 (Dec.) 1932.

Siegmann discusses the literature and reports twelve cases that occurred in Hajek's clinic between 1926 and 1931 and a few others. The series comprises: five cases of inflammatory infiltration of the wound; one case of pneumonia with inflammation of the wound, followed by otitis; four cases of peritonsillar abscess; four cases of parapharyngeal or retropharyngeal abscess, and one case of infiltration toward the mediastinum. The author thinks that these postoperative inflammatory complications can probably be attributed to faulty anesthetizing technic, consisting in an injection into diseased adenoid tissue or the carrying of bacteria from the surface of the mucosa into the submucous tissue with the hypodermic needle. By injecting too deeply one may cause local infection either of the pharyngeal musculature or of the parapharyngeal space (by piercing the pharyngeal wall), with danger of spread in several directions, particularly toward the mediastinum. The author emphasizes the importance of waiting four weeks after the last attack of tonsillitis.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

DIAGNOSTIC SIGNIFICANCE OF THE BLOOD PICTURE IN COMPLICATIONS OF PURULENT OTITIS MEDIA. J. SPIRA, Monatschr. f. Ohrenh. **67**:28 (Jan.) 1933.

On the basis of personal study Spira arrived at the opinion that the blood picture in uncomplicated acute purulent otitis media and that in the various complications of otitis media are not sufficiently characteristic to permit differentiation between them. On the other hand, the leukocytic formula is an important clinical symptom which in some cases helps to simplify diagnosis. This applies particularly to thrombosis of the sigmoid sinus or jugular bulb. A marked deviation in the leukocytic picture in otitis media when the results of internal examination are negative and there are no meningeal symptoms strongly suggests disease of the sinus or bulb. The absence of such a change makes this complication appear improbable, but does not exclude it. The blood picture has no significance as an indication for surgical intervention in mastoiditis.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

CALCINOSIS UNIVERSALIS. BARNEY J. HEIN, Arch. Surg. **26**:389 (March) 1933.

A case of diffuse deposition of calcium in the fascias is presented in a child, aged 6½ years. There were indurated areas in the upper and the lower extremities. Roentgen examination showed calcareous deposits in various parts of the body. The blood calcium was 16 mg. in February, and 10 mg. in August. The child recovered with the use of heliotherapy, and progressive roentgenograms showed a gradual disappearance of the calcium. KAISER, Rochester, N. Y.

PINK DISEASE TREATED BY LARGE DOSES OF FRUIT JUICE. HOWARD B. GLADSTONE, Practitioner **130**:610 (May) 1933.

Gladstone presents the case of a girl, aged 19 months, who, after being treated for pink disease for seven weeks with no improvement, showed marked, rapid improvement when two of her 5 ounce (150 cc.) feedings of milk were replaced by two 5 ounce feedings of fruit juice (composed of the juice of four oranges and one apple). The patient gained 22 ounces (623.7 Gm.) in the first two weeks and 34 ounces (963.88 Gm.) in the next four weeks. During the entire stay in the hospital, the patient was given treatments with infra-red rays daily and with ultraviolet rays twice a week. SAPPINGTON, San Francisco.

RAYNAUD'S DISEASE IN AN EIGHT YEAR OLD CHILD. MARTIN GONZALEZ-ALVAREZ, Pediatría españ. **22**:97 (Feb.) 1933.

Raynaud's disease, which is so rare in childhood, occurred in a child of 8 years. The first symptoms appeared at the age of 6 and began with severe pain in the affected extremities. The pain was followed by inflammatory manifestations and edema. Rose-colored, wheal-like spots were general over the body. The skin was very dry. Infarcted areas developed proximal to the painful regions. The lesions at times showed regression of symptoms followed again by exacerbation. The Mantoux reaction was strongly positive. The Wassermann reaction was negative. The typical picture of Raynaud's disease with loss of three end phalanges of the right hand and two of the left hand finally developed.

The roentgenologic thoracic findings indicated extensive tuberculous involvement. Application of both dry and moist heat gave relief to the extreme pain in the affected extremities.

The author advocates radiotherapy over the suprarenal regions. The ultimate prognosis in these cases is very grave. SCHLUTZ, Chicago.

SCLERODERMA AND ITS PATHOGENESIS. HANS SELYE, Virchows Arch. f. path. Anat. **286**:91, 1932.

Before describing the clinical picture of scleroderma, the author gives a historical introduction to the disease, which was known even to Hippocrates and Galen. This is important because it contains the recognition of sclerema neonatorum as a different entity. In the clinical picture there are the different stages: the edematous, the indurative and the atrophic. Pathologically, the increase in connective tissue is not confined to the skin but involves the blood vessels, muscles, bone marrow and, perhaps, more or less, all the organs of the body. In addition, depositions of calcium salts have been observed by numerous observers. There are at present many theories which attempt to explain the condition, such as the vascular, nervous, traumatic, infectious and rheumatic theories, and those based on the influence of cold, hyperthyroidism and hypothyroidism and suprarenal insufficiency.

Nursing rats, aged from 7 to 14 days, were given from 5 to 10 units of parathormone daily for three or four days, a total of from 15 to 40 units. Twenty per cent of the animals suffered from typical scleroderma, whereas the rest did not

show any signs of disease or remained backward in growth and died with more or less nonspecific signs of disease (for the most part pneumonia). Just as in the human being, three stages could be distinguished. On the day after the second injection, the skin of the neck and shoulder began to swell and was painful. The next day the edema had disappeared, and in its place a flat, indurated plate of hard skin which increased in size during the following days could be felt. The parts of the skin involved were symmetrical; soon the hair fell out, and ulcers appeared which healed with the formation of crusts. Then the skin became movable again and thin (atrophic stage). If the injections were given for only five days, the skin returned to normal after three weeks, and after two months the fur was that of a normal animal. The histologic picture, which seems to be similar to that of scleroderma in human beings, is illustrated by several histologic sections of the skin, which frequently shows deposition of lime salts in the necrotic areas. Infiltration of the nerves and small vessels of the skin and muscles with small round cells was observed in further analogy to the disease in human beings. The author therefore concludes that the experimental disease is analogous to scleroderma in human beings. He realized, however, that there may be other factors influencing the condition, since he could produce it only in 20 per cent of the animals. He wishes to classify scleroderma with osteitis fibrosa cystica and Albers-Schönberg's disease, since all of them are apparently due to a hyperfunction of the parathyroid glands. The possible practical importance of this point of view is considered. An extensive bibliography is given.

SCHOENTHAL, New York.

DIPHTHEROID OF THE SKIN. S. BAGDANOV and K. GAVRILOV, Sovet. vestnik venerol. i dermat., no. 9-10, p. 37, 1932.

The authors report a case of a 17 year old boy who complained of a painful ulceration in the anal region, painful defecation and general weakness of one week's duration. The ulcer was superficial and was 4⅘ by 6 inches (12.2 by 15.2 cm.) in size. Its borders were soft, and the base was uneven. The ulcer bled easily and was covered with grayish-greenish matter. Bacteriologic examination revealed only diphtheroid bacilli which morphologically could not be differentiated from diphtheria bacilli. However, different biologic tests such as the virulence test on the guinea-pig, the effect on carbohydrates, the agglutination test and the negative effect of diphtheria antitoxin on the patient proved that the ulcer contained diphtheroid and not diphtheria bacilli.

BLOOM, New York. [ARCH. DERMAT. & SYPH.]

SANTONIN AND ERYTHEMA. K. A. ROMBACH, Nederl. tijdschr. v. geneesk. **77**:519 (Feb. 4) 1933.

The author describes two cases of erythema produced by santonin in which there were no symptoms of poisoning. Recognition of the condition was made difficult by its resemblance to scarlet fever and by the lack of knowledge of erythema caused by santonin. Further considerations of the literature are presented.

VAN CREVELD, Amsterdam, The Netherlands.

Surgery and Orthopedics

CLEFT-PALATE PROCEDURES: EXPERIENCES AND OBSERVATIONS. IRVING WILSON VOORHEES, Arch. Pediat. **50**:73 (Feb.) 1933.

Voorhees gives certain rules which, if followed, will insure more satisfactory results in operations for cleft palates. Operation is advisable between the twentieth and twenty-fourth month, before the child has acquired speech. Patients should be properly selected with reference to general health and to obvious sources of infection such as the tonsils, adenoids and sinuses. Postoperative inspection and

properly supervised nursing are necessary. Certain technical points concerning the usual operation for cleft palate are described. WADDELL, JR., University, Va.

URETERODURAL ANASTOMOSIS FOR THE TREATMENT OF HYDROCEPHALUS. LEO M. DAVIDOFF and FREDERIC W. BANCROFT, Arch. Surg. **25**:550 (Sept.) 1932.

The case of a child, aged 21 months, with a so-called communicating hydrocephalus is reported. The operation performed, which has been previously reported by Heile, consisted in a unilateral nephrectomy followed by anastomosis of the upper end of the ureter, with an opening in the lumbar dura mater. The outcome of this case was fatal. Observations made at autopsy are reported.

KAISER, Rochester, N. Y.

RÔLE OF INFECTION IN THE PRODUCTION OF POSTOPERATIVE ADHESIONS. GEORGE P. MULLER and LEE A. RADEMAKER, Arch. Surg. **26**:280 (Feb.) 1933.

Experiments on animals (guinea-pigs) showed that postoperative adhesions occurred when infection existed during the primary operation. A clinical survey of forty-two patients operated on for symptom-producing postoperative adhesions revealed that at the time of the original operation only two had no evidence of wound infection.

The authors conclude that intra-abdominal infection and wound infection are primary factors in causing symptomatic adhesions for which secondary operations are necessary.

KAISER, Rochester, N. Y.

PRACTICAL POINTS APPLICABLE TO ANAESTHESIA IN CHILDREN. HAROLD SINGTON, Practitioner **130**:441 (April) 1933.

The author discusses the subject of anesthesia in children from the psychologic and the physical points of view. He feels that it is essential for the peace of mind of the child that induction be approached with the greatest care and tact in order to avoid panic or fear during the process. The author uses paraldehyde for the premedication in children. The dosage used is 1 drachm (3.9 Gm.) for each stone (6.4 Kg.) of body weight. This is administered in a small amount of saline solution by rectum. It is advisable to begin the administration two hours before the time of operation. The patient is usually asleep within forty minutes and hence does not resent the hypodermic injection of atropine. For induction, Sington uses a preparation of ethyl chloride with alcohol. He has used it in more than 60,000 inductions in children and feels that it is perfectly safe when properly administered. Following the induction, ether is administered. With this method patients usually sleep after the operation for from six to twelve hours. The technic of each procedure is described in detail.

SAPPINGTON, San Francisco.

PEPTIC ULCER IN MECKEL'S DIVERTICULUM. G. SCHAAFF, Deutsche Ztschr. f. Chir. **238**:78, 1932.

Gastric mucosa was found in six of fifty cases of Meckel's diverticulum, and occasionally in omphalomesenteric cysts and fistulas. Hydrochloric acid and pepsin have been found in such cases, which indicates normal function as well as normal structure of the gastric mucosa. The ulcers present were similar histologically to gastric ulcers, and in one case the free hydrochloric acid was 40, and the total, 70. The clinical history so closely simulates that of gastric or duodenal ulcer that preoperative diagnosis is difficult or impossible. The aberrant gastric mucosa secretes simultaneously with the stomach, and therefore pain appears soon after meals and is relieved by the alkaline intestinal fluid. The most constant features

of the condition are massive hemorrhage, bright red and often dark stools, colicky pains and severe peritonitis if perforation occurs. STEWART. [ARCH. PATH.]

TREATMENT OF EMPYEMA IN CHILDHOOD. ROSEMARIE BRANN, Monatschr. f. Kinderh. **57**:326, 1933.

In 125 cases of empyema in children, the mortality was 51 per cent for the first year, 31 for between 1 and 2 years of age and 4.6 per cent for over 3 years. The treatment recommended is repeated punctures independent of the nature of the organism. Following the subsidence of the acute infection, if the symptoms have not disappeared under repeated punctures, a rib resection is performed with the patient under local anesthesia, with closed drainage. The average duration of treatment is six and a half weeks.

Of 64 patients treated with this delayed operation, 89.1 per cent recovered, and 10.9 per cent died. GERSTLEY, Chicago.

THE SURGICAL TREATMENT OF SCOLIOSIS. H. VAN DER UPWICH, Maandschr. v. kindergeneesk. **2**:352 (April) 1933.

The mortality resulting from the surgical treatment of scoliosis is a little more than 2 per cent and is principally caused by shock. The end-results of surgical treatment in seemingly hopeless cases of scoliosis appear to be so good that the serious operative intervention seems to be fully justified.

VAN CREVELD, Amsterdam, The Netherlands.

SUBLUXATION OF THE RADIUS (PRONATION DOULOUREUSE) IN CHILDREN. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **76**:4210 (Sept. 3) 1932.

Subluxation of the radius, which is caused in young children in most cases by pulling suddenly at the arm, and which the French call *pronation douloureuse,* is explained as the result of the free upper edge of the radial head being caught in the narrow ligamentum annulare. The fixed pronation of the forearm after the trauma can be explained by the anatomic structure of the radial head, as the subluxation and the pinch are easiest brought about when the radial head is in pronation. Why this injury is more frequent in children cannot be explained by the typical structure of the radius and the ulna at this age.

VAN CREVELD, Amsterdam, The Netherlands.

OSTEOCLASIS OF CONGENITAL CLUBFOOT. J. P. KRUIMEL, Nederl. tijdschr. v. geneesk. **76**:4735 (Oct. 8) 1932.

After the treatment of twenty patients from 2 to 8 years of age with neglected and persistent clubfoot by means of osteoclasis, the author prefers this method to others because it is of short duration and afterward the children are less disturbed by pain. VAN CREVELD, Amsterdam, The Netherlands.

THE TREATMENT OF CHILDREN WITH HARELIP. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **76**:5557 (Dec. 3) 1932.

The author has observed about eighty cases. The unexpected difficulties which the family physician has to face when a child with harelip is born, as to choosing the time of operation and the manner of feeding, are discussed in detail. The author gives some technical details and helps in operative treatment which experience has taught are of importance. Finally, the possibility of operative correction of the results of the primary operation, which for various reasons may be imperfect, is stressed. VAN CREVELD, Amsterdam, The Netherlands.

Miscellaneous

METHYLENE BLUE AS AN ANTIDOTE TO CO POISONING. MATHILDA MOLDENHAUER BROOKS, Am. J. Physiol. **104**:139 (April) 1933.

Injections of methylthionine chloride, U. S. P. (methylene blue) into rabbits before or after the administration of carbon monoxide gas showed definitely that methylthionine chloride is an antitode for carbon monoxide poisoning, according to previous findings.

NOURSE, Cleveland.

DETERMINING INDIVIDUAL DEVELOPMENT. I. NEWTON KUGELMASS, Arch. Pediat. **50**:81 (Feb.) 1933.

Kugelmass deplores the present-day tendency to make all children live up to certain standards of mass measurement. He believes that attempts to standardize plastic youth into average patterns are physically detrimental to growing children, disturbing to parents and biologically false to the national ideal. He points out that children are individuals in the build of their body and in their organs and tissues, even to the single cells that compose the human structure. He points out in considerable detail why it is useless and improper to attempt to make children conform to standards.

WADDELL, JR., University, Va.

COMPARATIVE MEXICAN INFANT AND MATERNAL MORTALITY STUDY. OLIVE B. CORDUA, Arch. Pediat. **50**:192 (March) 1933.

Cordua presents a statistical study of 1,327 deaths in infants under 1 year of age, 200 deaths in children between the ages of 1 and 2 years and 129 maternal deaths.

WADDELL, JR., University, Va.

THE PRODUCTION AND PREVENTION OF DENTAL CARIES. MARY CALDWELL AGNEW, GORDON AGNEW and FREDERICK F. TISDALL, J. Pediat. **2**:190 (Feb.) 1933.

The appearance of dental caries in rats fed various diets was studied. Seventy of 71 animals fed a diet low in phosphorus and vitamin D showed dental caries. The addition of vitamins A, B, B_2, C and E to this diet had no apparent effect on the teeth. The addition of phosphorus prevented dental caries in 4 of 7 rats, and the addition of vitamin D prevented caries in 6 of 19 rats. The amount of calcium in the diet had no demonstrable influence on dental caries. In 365 rats fed a completely adequate diet no dental caries was observed. The authors conclude that in the rat an adequate amount of phosphorus is an important factor in preventing dental caries, and that, although vitamin D may prevent or delay the onset of caries, it is not as important as phosphorus.

LEMASTER, Evanston, Ill.

THE NEW LEGAL ORDER CONCERNING EDUCATION IN THE CARE OF INFANTS AND SMALL CHILDREN. E. THOMAS, Arch. f. Kinderh. **93**:266 (June 16) 1931.

Thomas discusses the recent regulation requiring one year's training for persons to be qualified as caretakers for well infants and children and two years' training for nurses of sick infants and children. The theoretical and practical subjects to be taught in this course of instruction are also discussed.

LEMASTER, Evanston, Ill.

Society Transactions

AMERICAN ACADEMY OF PEDIATRICS AND CENTRAL STATES PEDIATRIC SOCIETY

Saturday Morning, Sept. 23, 1933

JULIUS H. HESS, M.D., *Chairman*

(Concluded from page 711)

EXTENSIVE OSTEOMYELITIS OF THE SKULL AND LEPTOMENINGITIS WITH RECOVERY. DR. B. M. GASUL, Chicago.

A boy, 7 years of age, was well until June 26, 1932. Then a swelling developed in the right nostril which extended along the right cheek and quickly involved the eye. Within two or three days the entire mouth, cheek and eye were swollen.

The first examination revealed an emaciated child, with legs flexed on the thighs, the thighs at a right angle to the body and marked rigidity of the neck. The Brudzinski and Kernig signs were positive. There were a Babinski sign and marked, sustained clonus of the left ankle, hypotonicity of the left side and paresis of the left facial nerve with puffy swelling of the frontal area. A roentgenogram showed diffuse osteomyelitis of the right frontal and parietal regions. Spinal puncture revealed pressure, ++++; Pandy test, ++++; the cell count, 620, and the colloidal gold curve, 0000013554. The frontal abscess was incised and Staphylococcus haemolyticus was found on smear. The diagnosis was osteomyelitis of the skull with pachymeningitis and leptomeningitis.

The temperature ranged from 105 to 99 F. for the next three weeks.

As usually happens in cases of thrombophlebitis, there was an exudation into the medullary tissue between the inner and outer tables of the skull. If an infection extends inside, it causes pachymeningitis, and if it involves the pia, it causes leptomeningitis. According to the literature, there is much discussion regarding cases like the one presented as to whether there is pachymeningitis first, which extends to the inner table of the skull and then to the outer table. The cases are few and the only way a diagnosis can be made is by necropsy. It is possible that through hematogenous spread there may be pachymeningitis first and then osteomyelitis. According to the report, the boy had meningitis from the time he entered the first hospital on July 1.

The prognosis was very bad. So far as my associates and I were concerned, we did not know of any patient in such a condition who had recovered. We see many cases of purulent meningitis at Cook County Hospital, and, of course, the patients all die. We decided to treat this patient conservatively by means of repeated spinal punctures.

The condition progressed well with a decreasing temperature and pulse until August 13, although there were signs of increased intracranial pressure. On August 13, a convulsion, jacksonian in type, developed on the left side. The child appeared to be smelling something constantly and had a projectile type of vomiting. Dr. Guttmann gave him a large dose of sodium amytal, and at that time it was decided that an operation should be performed.

An operation was performed on August 14 by Dr. Beck and Dr. Guttmann, at which time they removed as much osteomyelitic tissue as possible. While the patient was on the operating table, his condition became grave and he appeared to be close to death. He was given fluids, gastric lavage and magnesium sulphate to relieve the intracranial pressure, and he revived. The signs of meningitis persisted with little change until there again were marked signs of increased intracranial pressure, with severe headache and projectile vomiting. The pulse was slower. The blood pressure on one occasion was 82 systolic and 40 diastolic and on another, 110 systolic and 84 diastolic. The patient had a definite left central facial paralysis

and paralysis of the left arm and leg. What was the cause of the paralysis? The first operation revealed indications of an abscess and now there were symptoms of an abscess of the brain or a subdural abscess. In either case, the thing to do was to operate again, before which we thought that a neurologist should see the patient.

Following this operation the child's condition improved. The vomiting stopped because the pressure was relieved; he did not complain so much of headache, and even the paresis was markedly improved, although he did complain of photophobia. Because his condition was improving and because he had been in the hospital so long, we thought that it would be a good plan to send him home, with the understanding that he was not entirely well and might have to return to the hospital. The patient was sent home on September 15, and we continued to do spinal punctures, for this was the only means of reducing the intracranial pressure. He got along well for a time until again signs of increased intracranial pressure developed, with an increase in the paresis and severe headache. The patient was operated on again and the rest of the osteomyelitic tissue was removed, and since then the boy has made a good recovery. This proved that the pressure was sufficient to cause the hemiplegia, for following the operation the hemiplegia gradually disappeared. The vomiting stopped, and the boy has gained in weight until he weighs more now than ever before, 53 pounds (24 Kg.), and has no definite symptoms of meningitis. He is now attending school.

I have presented a case of extensive osteomyelitis of the head, probably on a hematogenous basis, with pachymeningitis and leptomeningitis in a boy, aged 7. Staphylococcus haemolyticus was found several times in the spinal fluid, in the pus from the abscess and in a smear from the dura. So far as I could tell from the pediatric literature and from the records at the Cook County Hospital, this is the first patient with a condition of this nature who has ever recovered.

LYMPHANGIECTASIS WITH CHYLORRHEA. DR. THOMAS P. SALTIEL, Chicago.

Because of the scarcity of cases on record and the interest which surrounds its pathogenesis, the following case of lymphangiectasis with chylorrhea is presented.

J. S., a colored boy, 12 years old, entered the hospital with a complaint of swelling of the upper part of the left thigh and an intermittent milky discharge from small vesicles the size of a millet seed in the left groin. The duration of the complaint was three years. During this time the left leg remained swollen, not varying a great deal in size on rising or retiring.

The case history was uneventful. The mother had two miscarriages after the patient was born. No history of tuberculosis was obtained. Positive physical findings consisted of a moderate generalized lymphadenopathy and an obvious disproportion in the size of the lower extremities. On the upper part of the left thigh, which was distinctly larger than the right, many small discrete vesicles were present. When one of the vesicles was punctured, a milky white fluid was discharged. This fluid, on chemical examination, proved to be chyle. Serologically, the Wassermann and Kahn reactions of the blood and chylous fluid were 4 plus; the reaction of the spinal fluid was negative, and the Mantoux test was negative. The patient received intensive antisyphilitic treatment for over a year with no abatement of the symptoms or change in the serologic reactions. Two months ago an exploratory laparotomy was performed, which showed many enlarged lymph nodes, especially marked about the small intestine. Histologically, these nodes showed changes characteristic of chronic lymphadenitis.

Numerous theories are offered to explain the condition. One author advanced the idea of a congenital defect in the anlage of the lymph spaces with subsequent dilatation caused by stasis and congestion. Another held to the idea of an abnormal communication between the lymph vessels of the thigh and chylous vessels on the same side. There is, too, the possibility of obstruction of the flow of chyle into the thoracic duct by a syphilitic or a tuberculous gland, producing dilatation of the lymph spaces in the upper part of the thigh. The pathogenesis of lymphangiectasis with chylorrhea is still an open question.

HYPOTHYROIDISM IN CHILDREN. DR. I. P. BRONSTEIN, Chicago.

In a recent publication I pointed out that the blood cholesterol value has definite possibilities as an aid in the regulation of therapy in children with a deficiency in thyroid function. I reported that the average blood cholesterol value, as determined by a study of twenty-five children in whom no known derangement of cholesterol metabolism was present, is 190 + mg. per hundred cubic centimeters of blood. This value coincides with the results of other investigators in the field.

The twelve patients studied at that time, of whom eight were boys and four girls, had blood cholesterol values, when not under treatment, ranging from 277 to 782. Thyroid therapy definitely lowered the cholesterol and effected clinical improvement in those children. Since that report was submitted twelve more children with hypothyroid function have been examined, making a total of twenty-four. In all these, hypercholesteremia was present when thyroid extract was not taken.

I shall now present brief notes on a number of these additional children, illustrating the clinical use of this blood lipid.

J. S., a girl, aged 10, was first a patient in the department when 6½ years old. During the period of absence she was supposedly receiving 4 grains (0.26 Gm.) of thyroid extract a day. For two months prior to her return visit she had received no extract. She gained considerable weight, the abdomen was large, the mentality was duller, the skin and hair were rough, the neck was bare, and the fingers were stubbed. The immediate impression was that of a cretin. Hospitalization was refused, and the child was too uncooperative for a study of the basal metabolism.

On May 2, 1933, the blood cholesterol was 556, and after several such high readings she was given thyroid extract, starting with 1 grain (0.065 Gm.) and increasing to 3 grains (0.19 Gm.) a day. Within forty-five days the cholesterol gradually fell to 192, and several determinations after the feeding of thyroid extract gave similar normal readings. In this period remarkable clinical improvement was effected.

M. R., a girl, 6 years of age, presented the complaint of coldness and sluggishness for a period of one year. She was small for her age and very slow. As evidence of her inactivity, she sat curled up in a chair most of the time. She had a large abdomen, with an umbilical hernia. Her voice was low and the tongue large, nevertheless, she was alert mentally. The birth and developmental histories were normal. Her case fell in the category of so-called juvenile hypothyroidism, the type that follows in the wake of the numerous childhood intoxications and infections.

The initial cholesterol reading was 625 in October, 1932. On active treatment with thyroid extract the values fell gradually, first to 325 and finally to 175 within a period of three months, and remained within normal limits until May, 1933. At this time, because of supposed overactivity, the dosage was cut down by her mother, whereupon the cholesterol rose to 263, and a return of a low voice and coarse hair was apparent.

L. B., a girl of 6, under treatment since she was 1½, had a normal intelligence quotient for her chronological age. Physically, she was not recognizable as a child with a deficient function of the thyroid gland. Her mental rating was unusual, since the mental progress seldom parallels the physical improvement. Her parents were anxious to stop the specific medication, because her condition was so improved. We were able to hospitalize her and to prove satisfactorily that discontinuance of the treatment for a period of even five or six weeks brought a return of the symptoms of hypothyroidism. She grew obese, her abdomen enlarged, and her mental processes slowed up considerably. On entrance her cholesterol reading was 200; after stopping the treatment it rose to 312, and on resuming treatment with the specific drug, the blood cholesterol fell and stayed within normal limits. The last few readings were 192, 185 and 161.

D. B., a girl, 15 months old, is the youngest cretin in the group. She had a normal birth and was breast-fed for three months. At 3 months breast feeding was stopped, and the mother observed that the child's voice grew weaker and was low, that the skin and hair were dry and that she was lazy in taking food and in her movements. She was suspected of being a cretin. A study of the basal metabolism was impossible, since no enclosed respiratory chamber was available. The initial cholesterol reading was 416. On receiving extract of the thyroid gland, starting with ½ grain (0.032 Gm.) and increasing to 1½ grains (0.097 Gm.) marked clinical improvement was noted. The mother remarked that her child was becoming normal "once more." The cholesterol readings gradually fell to 333, 312, 227, and the last few readings have been normal: 208, 179 and 147.

R. S., a boy, aged 4½ years, was referred to the hospital for examination for hypothyroidism because of obesity, torpor and poor reaction to his environment. He was observed for four or five weeks, during which time his blood cholesterol, taken every other day, was always normal. On taking thyroid extract he showed the increased activity of any normal child receiving this medication. The study found him to be alert and in no way a child with deficient function of the thyroid gland.

G. M., a boy, aged 6½ years, hitherto described, shows strikingly the relationship of the cholesterol to the basal metabolism and the dosage with thyroid extract. I shall present a slide bearing out these relations.

I have by means of clinical material shown the use to which cholesterol was put in following the progress of treatment in a group of children.

When it is impossible to determine the basal metabolism in older thyroid-deficient children on account of unmanageability, mental retardation or fright, or in infants because of lack of respiratory chambers, cholesterol readings may serve as a contributing aid. Clinical impressions and basal metabolic rates, as ordinarily determined, have definite limitations, and therefore blood cholesterol may serve as a valuable adjunct.

MYOTONIA CONGENITA (THOMSEN'S DISEASE). DR. H. G. PONCHER, Chicago.

A sporadic case of myotonia congenita (Thomsen's disease) is presented, in which the patient was successfully treated. The patient was a white boy, 5 months old, with a definite history of onset at the age of 5 weeks. Myotonia was present in all the voluntary muscles of the body, including the tongue, pharynx, larynx, diaphragm and accessory muscles of respiration. The outstanding clinical manifestations were difficulty in nursing, severe cyanotic attacks associated with generalized tonic spasms and prolonged musculature contraction. The muscles gave the classic myotonic reaction described by Erb, and marked generalized muscular hypertrophy was present. Biopsy of the muscle showed normal structure.

A defect in creatine metabolism was found on study of the metabolism and served as the basis for successful therapy with thyroid extract.

Dr. Poncher gives the rationale of the treatment, and raises the question as to whether the disease does not occur more frequently than is recorded in the literature.

CHONDRODYSTROPHY AND OSTEOGENESIS IMPERFECTA. DR. R. H. JAFFÉ, Chicago.

Recently, a monograph revived the old theory first advanced by Glissen, that chondrodystrophy is a form of fetal rickets. Of course, this concept will cause a great deal of discussion. Therefore, it is of interest to see a classic specimen of chondrodystrophy, from which it is apparent that it does not fit into the conception of fetal rickets. This condition occurs in families, it is hereditary, and it occurs in some parts of the world where rickets is practically unknown. This specimen is a premature infant, expelled spontaneously at eight months. It is one of twins, and the other child is normal. That is against the concept of fetal rickets: Why should one twin be affected and not the other? Here we see the

shortness of the extremities, the heavy abdomen and the cretin-like expression of the face. The essential lesion was maldevelopment of the cartilage. Ossification stopped, and the bones were very short. The bones are firm, hard and essentially abnormal; they did not grow, and they are very compact. In this condition there is no evidence of hypofunction or hyperfunction of the endocrine glands.

Sometimes there is difficulty in distinguishing between chondrodystrophy and osteogenesis imperfecta. A study of the two specimens shown here will show the difference. In chondrodystrophy the extremities are much shorter than in osteogenesis imperfecta, the skin is thick, the abdomen is large, the thorax is short, and there are peculiar deformities of the extremities. In osteogenesis imperfecta the skull is soft and flabby, and the underlying condition is entirely different from that of chondrodystrophy. The ossification is normal; therefore, the bone marrow is normal. The bones are long and thin and very frail. The slightest movement causes the bones to break, and fractures are characteristic of osteogenesis imperfecta. The shortness of the bones is due to fractures in utero, but the fractures heal and callus forms. There are sufficient osteoblasts, and the fractures heal like any other fractures.

In chondrodystrophy, the shortness of the extremities is due to a disturbance of enchondral ossification, and the bones are firm, hard and compact, and there are no fractures; the lower extremities face away from each other. In osteogenesis imperfecta the bone is thin and frail, and there are many fractures, and the lower extremities face each other.

Osteomyelitis of the Maxilla and Mandible in the New-Born. Dr. H. G. Poncher and Dr. J. R. Blayney, Chicago.

This article will be published in full in a later issue of the American Journal of Diseases of Children.

Paregoric Dosage for Infants. Dr. Henry E. Irish, Chicago.

Prompted by the wide variation of published dosage of camphorated tincture of opium (paregoric) for infants, this study of observations of 297 infants was made to determine, if possible, what doses are effective and safe.

Having repeatedly observed total absence of effect from doses in the advised amounts in infants, I gave a group of infants under 1 year of age doses based on body weight, starting as 1 minim (0.06 cc.) per pound (453.5 Gm.) four times a day at intervals of four hours before feeding. These doses were increased 1 drop a day until 5 minims (0.33 cc.) per pound were given four times a day. By computation it will be seen that with the largest dose, an infant weighing 6 pounds (2,722 Gm.) received 30 minims (1.99 cc.) four times a day and an infant weighing 17 pounds (7,711 Gm.), 85 minims (5.61 cc.) four times a day.

Doses of 5 minims of paregoric to each pound of body weight produced no change in the pupils and no toxic signs. The drug increased somnolence and caused some infants under 4 months of age to become drowsy.

Frequency in stools was reduced in some infants with doses of 1 minim to the pound. Infants under 4 months of age were slightly more affected, as indicated by drowsiness, than those over 4 months.

Full physiologic effects without signs of toxicity were elicited with morphine administered hypodermically in doses of $\frac{1}{600}$ grain (0.0001 Gm.) to the pound.

This dose is practically the same in relation to weight as the adult dose. It is far below the toxic dose of $\frac{1}{150}$ grain (0.0004 Gm.) to the pound. Idiosyncrasies in the direction of increased resistance to the action of the drug but not in the direction of increased susceptibility were noted. Many physicians use no opiates in the treatment of infants, because they have knowledge of satisfactory substitutes.

The establishment of a safe upper limit for doses of paregoric and morphine is useful in exact therapy.

OXYGEN UNIT FOR PREMATURE AND VERY YOUNG INFANTS. DR. JULIUS H. HESS, Chicago.

The oxygen unit for infants is designed to convert the Hess heated bed into a chamber for oxygen therapy. When oxygen therapy is indicated, the oxygen unit replaces the cover and canopy supplied with the bed and forms an oxygen chamber of a size to accommodate conveniently infants up to about 6 months of age. The unit was designed primarily for premature and young infants in the obstetric nursery and in infant wards and stations.

It meets the special indications of oxygen therapy in asphyxia after resuscitation in the new-born, cyanosis in young infants from various causes and various pulmonary infections. In a few instances in which a mixture of oxygen and carbon dioxide is indicated, this combination may be substituted for the oxygen.

The ordinary large commercial tank of oxygen contains a little more than 200 cubic feet of oxygen and should last about forty-eight hours, using 2 liters per minute.

Two liters of oxygen per minute will maintain an oxygen concentration within the bed, varying from 38 to 80 per cent, depending on the amount of air which is allowed to mix with the oxygen as it passes through the flow meter. During the first twenty minutes, when preparing the bed for use, 4 liters of oxygen per minute may be needed temporarily. This also may be true for patients with marked respiratory embarrassment, if the door into the feeding room or dressing room has been left open for a prolonged period.

With the temperature of the room and bed at 80 F. and the bed empty and a flow of 2 liters of oxygen per minute the desired oxygen content will be established within the bed in thirty minutes. With the flow meter set at 0 the content inside the bed will be from 70 to 80 per cent oxygen; set at 1 the content will be from 50 to 55 per cent oxygen; at 2, from 40 to 45 per cent, and at 3, from 38 to 42 per cent.

A 38 to 42 per cent oxygen-air mixture answers most indications for increased oxygen. This about doubles that in the air under ordinary living conditions. When emergency stimulation for a short period is indicated, a higher percentage of the oxygen mixture may be needed for purposes of resuscitation.

With premature and young infants born at full term, the humidity within the bed does not become excessive while there is a free flow of the oxygen-air mixture. For the premature infants it may even be necessary to warm the bed temporarily to as high as 90 F. or more.

In the case of larger infants and those with fever, the procedure to be adopted to control the relative humidity is to fill the ice tank with a mixture of crushed ice alone every three hours for larger infants, up to 2 or 3 months of age, or ice with coarse salt every two hours for older infants and infants with fever. With older infants and those with a high fever, the temperature of the bed is raised materially. By using the ice tank the temperature of the bed can be maintained at practically the same degree as the temperature of the room, or at least within a variation of from 3 to 5 degrees. With the ice tank filled, there is a drop in humidity approximating 10 per cent in the two hours.

The newer models of the bed are now equipped with stopcocks and nozzle attachments, whereby a connection of rubber tubing can be made directly with a faucet and outlet so that the bed can be cooled by a flow of water without the use of ice.

In none of the experimental tests with premature, full term new-born or older infants, or those ill with pneumonia, did the content of the chamber show a percentage of carbon dioxide to exceed 1 per cent. The carbon dioxide usually reached a definite level by the end of the first hour and then remained fairly constant throughout the period that the infant was in the chamber.

Of 289 infants admitted to the station for premature infants during the first year after the oxygen beds were installed, and of which 256 were infants born prematurely, 128 of the total number presented symptoms which we thought would be benefited by the administration of oxygen.

The pathologic conditions in this group of infants were: marked atelectasis 15, of which 10, or 66.6 per cent, died; intracranial hemorrhage, 45, of which 19, or 42.2 per cent, died; pneumonia, 23, of which 7, or 30.4 per cent, died; miscellaneous, 45, of which 15, or 33.3 per cent, died. Among the 51 who died, 37 died within twenty-four hours after admission. Many of these were fetuses of 6 or 7 months.

Most of the infants who lived were in the oxygen bed for more than twenty-four hours. Except in a few special instances, the infants were kept in a 40 per cent oxygen atmosphere (ordinary air is 20 per cent). In a few extreme cases this was increased to from 50 to 55 per cent for short periods, for the purpose of resuscitation. In a very few cases, in which the mother had received morphine-scopolamine anesthesia, resulting in a toxic state in the infant, a mixture of carbon dioxide 5 per cent and oxygen 95 per cent was used.

Up to this time during the second year, 48 infants have been admitted to the station and 23 (47.9 per cent) of these infants were placed in the oxygen bed. It is our custom to put all premature infants weighing under 1,200 Gm. in the oxygen bed for twenty-four hours after admission, even though they are not cyanotic, because of the more or less generalized atelectasis present in these small infants.

Histories of Nine Infants Who Died

Age on Admission	Weight at Birth, Gm.	Weight on Admission, Gm.	Infant	Time in Station	Autopsy Observations
12 days	.....	1,750	Twin	40 hours	Intracranial hemorrhage
6 days	.....	1,435	Twin (colored)	18 days	Atelectasis, athrepsia, otitis media
New-born	947	.....	Placenta praevia	9 hours	Atelectasis, fracture of right clavicle
New-born	1,275	.....	Triplet	48 hours	No autopsy (clinical symptoms: shallow respiration, cyanosis, marked clonic spasm)
New-born	1,485	.....	Triplet	24 hours	Atelectasis and melena
New-born	1,430	.....	.....	13 hours	Atelectasis
New-born	1,120	.....	Placenta praevia	24 hours	Atelectasis
New-born	1,430	.....	Twin	22 hours	Cerebral hemorrhage
2 days	.....	1,680	Placenta praevia	72 hours	Atelectasis

Nine of the 23 infants (39.1 per cent) died.

Among those who recovered were 4 weighing at admission, respectively, 970, 790, 890, and 865 Gm.

The weights of the 48 infants on admission were: 5 under 1,000 Gm.; 12 between 1,000 and 1,500 Gm.; 24 between 1,500 and 2,000 Gm.; and 7 between 2,000 and 2,500 Gm.

NEUROCYTOMA DERIVED FROM A GANGLIONEUROMA OF THE HYPOGASTRIC PLEXUS. DR. SAMUEL J. HOFFMAN, Chicago.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

THE SIGNIFICANCE OF TREMORS IN THE NEW-BORN. DR. M. P. BOROVSKY and DR. P. L. ARIES, Chicago.

Our attention was directed to certain babies who have coarse, bilateral, forceful tremors of the extremities, usually of the upper extremities, although at times both the upper and lower extremities are involved. The tremor lasts from a few seconds to half a minute. It may be initiated spontaneously or started by mild stimuli such as tapping the soles of the feet. The symptom is noted on the first day of life and persists for from two to four days. The great majority of infants

show no tendency to have such tremors at any time. Most of the cases occurred in infants born after difficult labors, in which operative procedure was followed or in which some toxemia of pregnancy had existed.

Forty new-born infants having tremors were observed. No other evidence of cerebral injury was found. In ten cases of cerebral hemorrhage, six patients had no tremors, but rather spasticity, flaccidity or spasmodic twitchings of muscle groups.

The spinal fluid obtained by cisternal puncture was examined in thirty-one cases. The fluid was either clear and xanthochromic or contained blood. When the bloody spinal fluids were rotated in the centrifuge tubes, the supernatant fluid was xanthochromic. The fluid was colorless in two instances. The pressure was usually increased.

The tremors occurred after all types of labors and deliveries, but particularly after deliveries in pathologic cases. Toxemia in the mother is an important predisposing factor. Our impression is that the tremors are due to cerebral concussion, hemorrhage or the action of toxins on the central nervous system. An infant having tremors should be kept under closer observation than the average new-born.

DEVELOPMENT OF INFANTS ON A DIET OF A SPECIAL CEREAL MIXTURE. DR. MAURICE L. BLATT, Chicago.

The diet prescribed by the pediatrician for the young infant seems well balanced. When Tisdall, three years ago, described a new cereal mixture containing farina, 53 per cent; bonemeal, 2 per cent; oatmeal, 15 per cent; dried brewer's yeast, 1 per cent, and alfalfa, 1 per cent, which was being marketed, I looked with skepticism on its advent as an adjuvant to the pediatrician's armamentarium. It seemed to me that the optimum in balanced feeding mixtures could be obtained through the adequate use of common foods to which the fat-soluble vitamins were added.

In order to determine the value of the addition or substitution of the new cereal in the infant's diet, a problem was conducted by Dr. I. E. Shapiro and myself with the assistance of Miss Sawby as dietitian and Miss Kortum and Mrs. Kluver as laboratory technicians. One hundred and thirty-six infants at St. Vincent's Infant and Maternity Hospital were observed over varying periods from a minimum of six weeks to a maximum of one year, beginning in August, 1931. Seventy of these were given no cereal except the new preparation, and sixty-six were given only the cereals that are usually fed to infants. The latter received none of the mixture described by Tisdall.

A record of weight, total length, stem length, circumference of the head, circumference of the chest, intercristal diameter and time of eruption of teeth was made. The observations were plotted at intervals of two weeks.

At the termination of the problem, the curves showed a decided advantage in favor of the group receiving the described cereal. They weighed more, and their total length was greater. The stem length of the group fed the special cereal was even greater than that of the controls. The special group showed measurements greater than the controls in circumference of the chest and the head. A comparison of the hemoglobin of the two groups shows a higher curve in those fed the special cereal. The incidence of infection causing a rectal temperature of 101 F. or over was 1.35 per infant in the group taking the new product and 2.18 in the control group, for the year. There were no deaths in either group.

The children eating the new cereal had an earlier eruption of teeth than did those in the control group. At the close of the problem, it was determined that the average age at which the special group had twenty teeth was 26.75 months, and this development was not reached in the control group until two months later. It is our conclusion that this cereal mixture offers definite advantages in the feeding of infants and young children.

THE DIAGNOSTIC REACTION TO TUBERCULIN. DR. JOSEPH GREENGARD, Chicago.

The purpose of this investigation was to evaluate several methods of testing with tuberculin in relation to each other. In this regard especial interest lay in two procedures which are comparatively new: (1) the use of a purified total protein tuberculin (T P T, Seibert) and (2) the evaluation of a percutaneous reaction with a tuberculin ointment devised by Loewenstein designated Dermotubin. To accomplish this, simultaneous reactions to tuberculin were determined in all children admitted to Cook County Hospital. On the right forearm an intradermal test was made with 0.1 cc. of a 1:100,000 solution of total protein tuberculin (Seibert), 0.001 mg. of purified protein tuberculin to the dose. On the upper portion of the left forearm in a corresponding area, an intradermal injection of 0.1 cc. of a 1:1,000 solution of Koch's old tuberculin in physiologic solution of sodium chloride was made, 0.1 mg. of old tuberculin to the dose. On the lower portion of the left forearm a Pirquet scarification test was made, the same undiluted old tuberculin being used, and on the thorax over the upper end of the sternum a Dermotubin test, Loewenstein's ointment being employed.

The results of the tests in 647 consecutive cases show that 185, or 28.6 per cent, of these children reacted to one or more of the tests and 111 to all tests. The total protein tuberculin test, done intradermally, proved to be the most sensitive, yielding 96.2 per cent of the total positive reactions in dosages one-one hundredth of that used in the Mantoux test with old tuberculin. The latter was used principally for purposes of control, since it has been shown by D'Arcy Hart to carry an error of only from 4 to 6 per cent in the negative diagnosis of tuberculosis. The Dermotubin test caused 152, or 82 per cent, of the total positive reactions, while the Pirquet test caused 117, or 63.2 per cent, of the positive reactions.

The conclusions drawn from these findings are that: 1. The intradermal reaction is best suited for routine hospital use and should supplant other methods for this purpose.

2. Total protein tuberculin (Seibert) is extremely sensitive, and will detect a higher percentage of positive reactions than old tuberculin in doses a hundred times as great.

3. The Dermotubin test is less sensitive than the intradermal test, but is extremely useful because of the ease and painlessness of its application. It is well suited to routine use in the office.

4. The Pirquet scarification reaction is greatly inferior to either the intradermal or the Dermotubin test. Either of the latter is therefore preferable for routine use.

THE PLANTAR REFLEX IN THE NEW-BORN. DR. CRAIG D. BUTLER, Chicago.

Because of controversy in the literature as to whether irritation of the sole of an infant's foot is characteristically followed by dorsal or ventral flexion of the toes, observations were made of 200 infants less than 10 days old, with the purpose of recording the predominate response and to determine, if possible, why there is so much discrepancy in the published data.

Two definite types of response were observed, viz., that elicited by light stroking of the sole and that provoked by pressure on the metatarsal pad. The former reaction depends on touch sensation, and the response is, in the great majority, extension of the great toe with more or less fanning of the other toes simulating the positive Babinski test seen in lesions of the pyramidal tract. The pressure reflex corresponds to the grasp reflex elicited by pressure in the palm of the young infant and consists of extreme flexion of all the toes.

The standard technic of the Babinski test, i. e., drawing a hard instrument along the outer border of the sole from the heel to the metatarsal arch and then across to the inner side, is apt to provoke a combined response both to touch and to pressure. To elicit the touch reflex alone pressure must be very light, and the response is usually best obtained when only the proximal half of the outer border of the sole is irritated. The force required varies with the patient and cannot be standardized. Usually, light stroking with the tip of the finger is sufficient, but

deep sleep, stupor from toxemia or trauma, or cold or dehydrated feet may make light scratching with the finger-nail or a hard instrument necessary. Care must be taken, however, to avoid a mixed response from deep pressure or a defense reaction to pain.

Four hundred and twenty-one tests were made on 200 babies, from two to four tests on different days being made on 140 babies. The babies were from ½ hour to 10 days old, the majority being under 6 days. The responses obtained were: pure extension of toes readily elicited in 73 per cent; pure extension of toes elicited with some difficulty, 10.5 per cent; atypical reactions in which extension predominated, 8.5 per cent; pure flexion of toes, 5 per cent; atypical reactions in which flexion predominated, 3 per cent; total extension responses, 92 per cent, and flexion response, 8 per cent.

No explanation was apparent for the flexion response in the 5 per cent or for the atypical reactions. Difficult delivery, hemorrhage of the brain and other pathologic states bore no constant relation to the type of plantar response.

Pressure on the metatarsal arch uniformly elicited flexion of the toes. In testing the plantar reflex, failure to avoid such pressure will result in a mixed response in which flexion will predominate.

RENAL INFANTILISM. DR. A. H. PARMELEE, Chicago.

W. K., a white boy, 10½ years old, was the first child of healthy parents, born by forceps delivery at full term. The weight at birth was 7 pounds and 13 ounces (3,543.6 Gm.). There were no signs of an injury sustained at birth, but he nursed very poorly, and on the thirteenth day his weight had fallen to 5 pounds and 2 ounces (2,423.6 Gm.). He never took food well during his infancy, but drank large quantities of water and passed a large amount of urine. At 6 months his weight was between 8 and 9 pounds (3,628.7 and 4,082.3 Gm.). He had an infection of the upper respiratory tract at this time, with suppurative otitis media. There was a convulsion during this illness. Shortly after this he had measles, and after that had frequently recurring infections of the throat and ears. Up to the time he was 14 months old he had taken no food except milk, orange juice and prune juice and had had no cod liver oil. Examination at that time showed a small, thin, flabby and pot-bellied child with enlarged epiphyses, a rachitic rosary and prominent frontal bosses, unable to sit alone. His weight was 15 pounds (6,803.8 Gm.), and his length, 25 inches (63.46 cm.). The urine was of low specific gravity and contained albumin, but no casts. When the child was 20 months old the tonsils and adenoids were removed because of recurring attacks of tonsillitis. During the night following the tonsillectomy he had a convulsion which persisted for two hours. The convulsion stopped immediately on the withdrawal of from 40 to 50 cc. of spinal fluid by lumbar puncture. When 2½ years of age he weighed between 19 and 20 pounds (8,618.2 and 9,071.8 Gm.) and his stature was very small. He could sit alone, but did not stand alone. He was mentally alert and seemed normally intelligent. He still drank large quantities of water and passed much urine, which was of low specific gravity and contained albumin, but no casts. He also still refused solid food.

During the last seven years the boy had not been acutely ill except for occasional infections of the upper respiratory tract, had grown slowly in stature and in weight, but had always remained very much below the average in size. He made fair progress in school. The polydipsia and polyuria continued. During the last two years of his life he showed increasing difficulty in walking and some awkwardness in the use of his hands. For several years the parents had noticed mental sluggishness during the winter months. In the last three months of his life he passed much less urine and showed considerable difficulty in urinating. About three weeks before his death he had a cold, accompanied by high fever and convulsions. I saw him two days after the onset and found him drowsy and apathetic, but talkative and apprehensive when spoken to or disturbed. The neck was not rigid, the eyes were normal, the tongue was heavily furred, the throat

and ears were normal, the lungs were normal, the heart was slightly enlarged to the left, the abdomen was soft, and the spleen and liver were not enlarged. The superficial abdominal reflexes were elicited with difficulty. No knee jerks were obtained, and a Babinski sign was present on the left side. There was ataxia of the arms and the legs. The blood pressure was 110 systolic and 60 diastolic. His condition grew steadily worse, and he died suddenly ten days after I saw him.

The essential pathologic findings in the postmortem examination were the extremely small kidneys, the right measuring 7.2 by 4 by 1.8 cm. and weighing 22 Gm., the left measuring 4.1 by 3 by 1.4 cm. and weighing 12 Gm. More than 90 per cent of the tissue was cortex. Histologically, the renal tissue showed marked dilatation of many of the convoluted tubules in the cortex, slight dilatation of the capsular spaces and an increase of cellular fibrils between many of the convoluted tubules. The general arrangement of the cortex was altered by the presence of septums that contained large blood vessels. The medullary portions were sparse, and there were only a few tubules that resembled collecting tubules, and most of these were surrounded by an increased amount of fibrous tissue. Both ureters were dilated, but straight and unobstructed from the renal pelvis down to their outlets into the urinary bladder. The urinary bladder was large, measuring 14 cm. in its maximum circumference at the fundus and 12.5 cm. from the internal urethral orifice to the base of the bladder. Its walls were very thick, from 5 to 6 mm. There was no obstruction to the orifices of the ureters or in any portion of the urethra from the prostatic portion to the external urethral meatus of the penis. The alterations in the kidney are interpreted as the result of a congenital anomaly in which the most prominent variation is an arrest of the development of the collecting tubules. The changes in the bladder are like those commonly associated with "cord bladder."

The striking clinical manifestations of this marked hypoplasia of the renal medulla were polydipsia and polyuria with albuminuria, anorexia, dwarfism, late development of uremic symptoms and the complete absence of arterial hypertension.

ENLARGEMENT OF THE LIVER. DR. C. G. GRULEE, Chicago.

L. S., an Italian boy, 3½ years old, was admitted to the Presbyterian Hospital on May 20, 1933. The child had had mild bronchitis for three months, but the only reason the mother brought the child to the hospital was because of enlargement of the abdomen. The history was irrelevant. So far as we could determine, the child had had an adequate diet.

Physical examination showed the child well nourished and well developed. The skin was sallow, the eyelids were puffy, the pharynx was somewhat reddened, and there was a slight nasal discharge. The lungs and heart gave no abnormal findings. The abdomen was moderately distended, and the edge of the liver was found within 2 cm. of the anterior part of the spine. It was smooth and rather sharp. The spleen was not palpable. The temperature was 99.8 F.; the weight, 35 pounds (15.9 Kg.).

Much to our surprise, the urine contained albumin, 4 plus, macroscopic and microscopic blood and some white cells. The blood showed slight leukocytosis, 17,000 cells, with mild anemia and hemoglobin content of 64 per cent. The Wassermann and Kahn tests were negative. The blood chemistry again offered a surprise in the cholesterol reading of 524.5. The other findings were negligible. The icteric index was 7.5, and the direct van den Bergh test was negative. The blood pressure was somewhat raised, but the other kidney tests showed no evidence of functional disturbance.

Since that time, the liver has gradually decreased in size, until now it is about 2 inches (5 cm.) below the costal margin. The slight palpebral edema soon disappeared, and the condition of the child has remained very much the same. During the past four months, there has not been much decrease in the amount of blood in the urine, but the general condition has not been disturbed.

My associates and I have considered two possibilities—von Gierke's disease and glycogenic hepatomegaly—without coming to a definite conclusion. In favor of the former condition are the urinary findings and the high cholesterol reading.

In favor of the latter condition are the marked enlargement of the liver, the high cholesterol reading and the high amylase content in the urine, which has gone as high as 100 units. On the other hand, the epinephrine test has been negative. The blood sugar has never been low. Acetone and diacetic acid have been found in the urine regularly.

Record of Studies of the Blood

Date	Cholesterol	Blood Sugar	Comment
5/22	524.5	95.7	
5/27	376.5	101.5	
5/27	.....	116.3	After epinephrine
6/19	592.5	76.9	
7/ 7	400.0	.....	
7/20	603.7	72.7	8:15 a. m. (fasting)
7/20	592.5	181.8	8:45, after epinephrine
7/21	410.2	88.5	8:30 a. m. (fasting)
7/21	420.9	76.3	12:30 (150 cc. of cream at 8:45)
7/21	533.2	76.6	4:30 p. m.
7/22	492.3	81.3	8:00 a. m. (fasting)
7/24	499.0	60.0	8:05 a. m. (fasting)
7/24	410.2	98.5	8:50 a. m., after epinephrine at 8:10
8/ 4	640.0	104.7	

CONGENITAL ABSENCE OF THE FIBULA. DR. HEYWORTH N. SANFORD, Chicago.

There were 213 cases of congenital absence of the fibula reported in the last article appearing in the literature in 1923. The etiology is presumed to be the pressure from too tightly fitting amnion or amniotic bands, between the fifth and eighth week of fetal life. The physical signs are characteristic. There is a sharp bend in the tibia, and over the bend there is usually a dimple in the skin, the so-called scar. The tibia is also shortened. The foot is in equinovalgus, and there is an absence of one or more toes. Some of the toes may be webbed. There is usually an absence of the external malleolus. The prognosis for good function is not very satisfactory. In a typical case the normal bones will not lend themselves to the construction of a foot even approaching the normal. The condition should be diagnosed, so that orthopedic treatment may be established before the end of the first year, as early use of the limb will prevent atrophy of disuse.

Two cases were presented with slides of the children as new-born and roentgenograms of the bones taken at this time.

CHICAGO PEDIATRIC SOCIETY

Annual Meeting, May 20, 1933

CHARLES SCHOTT, M.D., *Vice President, in the Chair*

Only one paper was presented at this meeting.

COPPER AND ANEMIA IN CHILDHOOD. PROF. DR. E. GORTER, Leiden, The Netherlands (by invitation).

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Regular Meeting, Oct. 17, 1933

CHARLES SCHOTT, M.D., *President, in the Chair*

PEDIATRICIANS AND MEDICOSOCIAL PROBLEMS. DR. CHARLES SCHOTT.

The pediatrician is not unlike the old time general practitioner in his closeness to the family group. The families rely on him for advice. They expect him to take leadership in the widespread movements in which they, through their

children, are interested. What could be more logical than that the pediatrician should take or assume the leadership in the problems or agencies of welfare that deal with measures for the betterment of children. These measures are often medical, but more often they are general social problems of welfare.

The pediatrician has permitted lay groups often headed by most laudably trained social workers to assume the direction of problems that rightly belong in the pediatrician's province.

We, pediatricians, belong to groups, whether they be fraternal or so-called service clubs, and many of them have as their leading welfare work the handicapped or underprivileged child, yet nowhere along the way have we given the organizations the ideas for their work, or have we assumed the leadership in this child welfare work.

It would seem that this might be a fitting time for the pediatricians to acquaint themselves with the social problems that are related to our specialty in medicine. We must not assume that our knowing the medical phase makes the social part of the work ours without some study. We cannot expect at once to take away the leadership and do the work of those who, during the period of lapse through which we have gone, have become real specialists in these respective works, but it is for us to take an active part in these works, and in some of the existing institutions to be looked on as interested if not as eventual leaders.

In the state of Illinois there are 7 state institutions, supposed to be eleemosynary, that deal with and care for children alone to the greater extent of their physical capacities. They are capable of caring for from 300 to 800 inhabitants, yet in only 2 of them are there physicians. These 2 are the institutions that deal not only with children. The other 5, 1 with 750 children as permanent guests and charges of the state, and the other 4 all having populations of over 500, have no resident physician. In all of these institutions the contract physicians who are in partial attendance are not particularly interested in children.

No pediatric group, or even a medical group, has been much interested in the conditions prevailing in these institutions. They have not shown any interest in how these children have been housed or fed. They have shown no interest in the character of the persons with whom these charges have come in intimate contact and under whose supervision the children have been and still are.

Only in 1 of these institutions—that for delinquent boys, where more than half are really only dependent youngsters—is there a pediatrician on the advisory board. This is the only one of the institutions referred to that has such a board.

In educational work in certain school problems the pediatrician should now be, or should have been, the agitator for proper teaching of all things, yet never has a pediatrician been on the school board of the city, or has his influence been felt in attempting to have sex subjects properly taught in the schools, though in most of them the most pronounced need exists.

The pediatrician's advice has not been asked, nor has he interested himself in any of the home finding or placement organizations.

Selfishly, we must make ourselves felt in all of the social movements that are dealing with us and with which we are in daily relations. It is for us to be the agitators for betterment in all of these existing institutions, so that we shall be called on when a new work is wanted, that we may suggest it or advise what should or should not be done. Let us make it known that these social problems and movements for betterment are the job of the pediatricians.

DISCUSSION

DR. C. A. ALDRICH: To my mind this paper is extremely important, for I think that the implications he has drawn apply closely to his original statements, and they explain the reason for the failure of the physician to regain his previous standing. I think that nothing physicians could do would accomplish this any quicker than study and work with the people who are busy in allied fields with children. To know anything about modern education we must work

with school teachers and get their point of view. We must know something about modern psychology and understand it, so that we can use it in our preventive work. To cooperate in the details of such work that is going forward in our different communities would be educational for us and would improve our standing locally.

AMERICAN ACADEMY OF PEDIATRICS IN THE STATE OF ILLINOIS. DR. GEORGE E. BAXTER.

The object of the Academy is to stimulate interest in pediatrics and to correlate all aspects of the work for the welfare of children which properly come within the scope of pediatrics.

The Academy is making a study of conditions and progress in all fields of child welfare activity and endeavors to be prepared through its various committees to furnish competent authoritative professional aid and guidance wherever these are wanted.

The state committee of the Academy for Illinois outlined its program and sought the advice and counsel of the educational committee of the Illinois State Medical Society and determined to work with the regular medical organization of the state.

The state committee of the Academy asked and secured from the officials of the Illinois State Medical Society, a section on pediatrics.

A subcommittee was appointed to contact with all governmental agencies in the state for the purpose of aiding or advising in matters pertaining to the welfare of children.

Another activity was the appointment of a subcommittee for the purpose of contacting with nongovernmental organizations in order to aid or advise these organizations in medical matters pertaining to other welfare activities.

Another activity was the organization of pediatric programs or postgraduate courses for county societies in the state and for branch societies in Chicago. This activity has met with a great amount of enthusiasm as expressed by those in attendance at six different district meetings in the state and at several branch meetings already held in Chicago.

The Academy of Pediatrics has committed itself to this program with the ultimate hope of creating a greater child consciousness in the minds of all practitioners of medicine with the hope that physicians will cease to be followers but will become leaders in all activities for the welfare of children. The slogan adopted to represent the idea is: "Every doctor's office a health center."

DISCUSSION

DR. M. L. BLATT: The Academy of Pediatrics is an attempt at organizing pediatric thought. It is an attempt to bring together a group that actually feels and thinks that the welfare of the child and of the family should be in the hands of persons who are trained for logical medical thinking. The work that Drs. Grulee, Baxter, Hess and Aldrich have done, the organizing of state-wide interest in pediatrics, is just the beginning of what may be accomplished in the state. The thoughts that Dr. Schott has expressed and the plans that Dr. Baxter has amplified are only those which, as all of us know, can be accomplished if we all work together.

DR. CLIFFORD G. GRULEE: About ten or twelve years ago a group was called together by the late Dr. John Dill Robertson to plan for immunizing all children against diphtheria. I was asked to speak at that meeting, and I raised a great deal of antagonism by saying that it was not a battle but a war, which it would take several years to carry through. What we are attempting now is something that must be continued over a series of years, and it must be very stubbornly fought.

Much that has been said tonight expresses what I have thought for a long while. I believe that the medical profession is getting together and is thinking more alike. The Academy has had two years of organization, first the national,

then the sectional, four sections in this country and one in Canada. Then came the development of the states, and I am happy to say that in Illinois the work is going ahead rapidly. It lagged for a while, but I think that within the last few months it has been going ahead rapidly with the things that need to be done. I am, of course, vitally interested in the Academy and in what it is doing. Many phases of the work will, perhaps, not appear on the surface. One of the things is the Board of Pediatrics that is being formed; if it were not for the Academy, the situation would have been chaotic, for we would not have had any one to form this Board. We were on the brink of having specialists certified by state boards of health; this would certainly have resulted in chaos. As it is, the Board of Pediatrics has got together.

I have had nothing to do with the organization in Illinois except to pat Dr. Baxter on the back and tell him that he is doing a good job. It is a good job. I have been present at two of the postgraduate meetings, and I was greatly surprised to see the interest the general practitioner is taking in this work. I remember one very hot day in Monmouth; the whole group sat through steadily from 2:30 in the afternoon until 10:30 at night, and but few men moved out of the room during that time, although the heat was terrific. We have the thing going now, and I think that it will go on. If we do not teach the members anything but consideration for pediatrics and the child, we shall have done an immense amount of good. As soon as we get the physicians aroused, we shall have the lay groups. It has not been as much a matter of lack of interest among the lay groups as among the medical groups.

DR. ARTHUR H. PARMELEE: It seems interesting to me that practically all of the movements which have been taken over by lay organizations and which are now fighting to get back under our control have arisen because the knowledge of the public has, we might say, gone ahead of the knowledge and interest of the medical profession. This is particularly true in regard to the care of the child. The mother is vitally interested in her child, and the origin of the movement for infant welfare was the direct result of this natural trend of events. The mother came to know more about the care of her child than the physician did. The mother found out after a while that problems of behavior are important, and she knew more about the psychology of the child than the general practitioner or the pediatrician did. Gradually these lay organizations have come back under the supervision of the medical profession, where they belong. As we go along, undoubtedly there will be other movements started by lay organizations because they are ahead of us in our knowledge, and I think that because of that fact we pediatricians need to be alert and to learn about these things before we find ourselves swamped by lay organizations dealing with new problems regarding which we should have been leaders. The work we have been trying to do in the state this summer under the auspices of the state committee of the Academy of Pediatrics—and I wish to call attention to the fact that all this work was done through organized medicine—is for the purpose of keeping the medical men of our state alert to what is going on, drawing their attention to the things they must know about the child. I have been to three of these teaching meetings. I freely admit that the first time I went I was rather skeptical about the way in which our attempt was going to be received, but after that first meeting I no longer had any fear that it might not be worth the while. It is astonishing the way the medical men of this state have responded and have enthusiastically received this gesture on the part of those who represent the state society and the Academy of Pediatrics. It seems to me to be a highly important movement.

DR. I. HARRISON TUMPEER: This is the first pediatric meeting that I remember in which the pediatrician has discussed himself. Out of the discussion has come the realization that we need a program devoted to pediatrics as the practice of pediatrics, more than one on the science of pediatrics. The science is so young and lusty that we still labor in the tradition of exclusively scientific programs. At first only the meetings of the medical society were plastered with pompous protocols. Now meetings of hospital staffs are stiff with sturdy statistics.

As Dr. Baxter emphasized, as students we are taught etiology, pathology and the other subdivisions and are never given any inkling that there is any more to the practice of the profession than the mere scientific phase. Our relations to the patient who has the disease are ignored. As practitioners, we continue to expect scientific programs exclusively and are blinded to the problems of practice. Our relations to the community which we serve are disregarded. As a result there has been a wholesale desertion of patients from the regular medical profession.

The situation seems to be as follows: The general practitioner is lacking in pediatric approach and thereby has lost a large share of practice to groups of lay organizations. The pediatricians of the state are supplying this lack by an excellent series of programs designed to renew the general practitioner's contact with the field. Although these postgraduate courses are valuable, the general practitioner of the future must be equipped in the medical school by means of appropriate courses covering the new phases of pediatrics. These courses must now include scientific nutrition, child psychology and problems of behavior.

I think that it is a fine thing to go out into the state and teach the general practitioner all about pediatrics in eight hours, but we are assuming that we know enough to teach all the subjects. We go out to teach the general practitioner, but who will teach us? One cannot become an authority by listening and reading. From my experience with the subject of allergy, to which I have devoted much time, money and study, I realize how superficially the average pediatrician touches the subject despite his glib utterances and casual attitude. The same must be true of the other subdivisions of pediatrics. Many of us have given lectures on problems of behavior with the ineffectual background of our often misleading practical experience and incidental reading.

I may be all out of order, but I should like to suggest a concrete way for the society to bring up the general level of its members with regard to the newer avenues in pediatrics. I suggest that the society devote itself this year to a course covering the special fields which we have neglected and which have become very important, as the discussion has indicated. The previous speakers have explained that the pediatrician has unfortunately divorced his realm from many important special fields, just as the general practitioner has excluded pediatrics as a whole. For instance, let Dr. Krafft or Dr. Beverly arrange a course for us in child psychology and psychiatry. Let other subjects such as scientific nutrition and posture be similarly treated. I suggest that a committee be appointed to consider this idea. It is logical. While we are attempting to widen the scope of the general practitioner, the scope of the pediatrician himself needs widening.

DR. HENRY E. IRISH: I have been quite interested in this meeting, and think that history is repeating itself. I recall that some years ago a group of us sent by the Illinois State Society to give pediatric programs had a happy experience along this line. The thing is now being done again, and even better than previously, and I am glad to see it. I think that the main reason why the men are interested in pediatrics is because they have been losing something by not being modernly equipped. Nearly every good-sized town has a pediatrician, and while the child population is about one fifth of the entire population, the pediatric phase of business for the general practitioner is about one third. It has interested the general practitioners to see this part of their practice going to the pediatrician, and they have wished to become more familiar with modern pediatrics because they do not wish to lose this part of their practice. Some years ago, I think some of you will recall, a meeting was held at the branch society, and Dr. Sanford was asked to address the assembly. We found that the general practitioners wished to complain about the encroachment of the Infant Welfare Society. Speaking in a rather querulous strain, I asked that from the members of the audience who condemned the work of the Infant Welfare Society those who had scales for weighing infants in their office raise their hands. One timid hand came up. That was the reason why they were not doing the work themselves. Many men are wondering why work on child behavior and psychology has been

taken away from them, but that is due to the fact that they know little about it. So with dietetics. How many of us have been using dietetics that are out of date? I think we can subscribe definitely to this as part of our pediatric work—and I think it should be a part of our work to be competent to advise those who come to us—we should not advance views that are so antiquated that the parents will go home thinking that our curative medicine is as obsolete as our behavioristic advice.

DR. C. A. ALDRICH: I think that to follow the suggestion of actually getting into these groups and working with them is the way to take care of that phase of the problem. A man cannot sit in a clinic for child guidance and listen without absorbing some child psychology, and he cannot sit in a meeting of a school board without absorbing something about education. If we could get appointments on these boards and committees, we could absorb a great deal of knowledge, and if we were careful not to talk too much in the beginning, we would not impair our reputations as men competent to advise in all matters relating to child welfare.

DR. GEORGE E. BAXTER: This discussion has brought out, with peculiar emphasis, the importance to all of us at times taking stock of our own educational necessities, the means to meet such a need, the ability of some to teach and the willingness of all to be taught. Dr. Tumpeer's remarks give food for thought. When physicians reach the point of self-satisfaction, they immediately begin to decline. When physicians refuse to give out helpful information and teaching to their fellow practitioners, they violate the highest ethical standards of medicine.

When this work was being started we met with some opposition; the word "teach" was not well received, so we changed to "pediatric program." A belief existed that there was an ulterior or selfish motive; it was stated that the general practitioners did not want the courses, and finally one pediatrician stated that it was bad economics for pediatricians to teach general practitioners to do work which would naturally take away practice from the pediatrician. This opposition gradually and, I am sure, wisely diminished to the vanishing point so that the majority of physicians in the state outside of Chicago are enthusiastic in their support of this program. Just a word about the work in Chicago, further confirming the remarks made by Dr. Grulee and Dr. Blatt. There have not as yet been enough meetings in Chicago to allow an estimate of the sentiment, but we are greatly encouraged by the cordial reception of the program by the branches.

This evening an invitation came from a branch, through one of our subchairmen, asking whether we could put on a program one week from tonight. It is only one week's notice, but already one of the teams has been assigned, and this branch will have the program. I think that there are fifteen branches, and we have already been asked to appear in more than half of them. Two have already had programs. In Chicago we have quite a good deal of work to do, quite as much or more than in the state. We are apt to look on Chicago as segregated from the rest of the state; it is in many ways, but all of the physicians are not pediatricians, and there is need for the physicians in Chicago to take charge of various lay organizations. Not only do we need to educate ourselves, but we must attempt to carry this matter of education to the different groups in the city of Chicago through the branch societies.

THE RELATIONSHIP OF HOME AND HOSPITAL IN THE MANAGEMENT OF SICK CHILDREN. DR. A. B. SCHWARTZ.

The Committee on Hospitals of the White House Conference on Child Health and Protection, of which Dr. Grulee was chairman, commented in its foreword on the changing character of children's hospitals. They are no longer simply asylums for the sick. The social values of the function of a children's hospital are still regarded with remoteness, particularly by interns.

In order to meet the needs of the present day the children's hospital must project its function outside its own physical walls.

The lantern slides shown exhibited results obtained in an intensive follow-up of cases of outpatients. These were part of a program undertaken at the Milwaukee Children's Hospital in 1930 and 1931. The effort was made to treat children in homes whenever it was possible to do so. As the mortality rates among hospitalized infants were high, treatment in the home in certain types of cases was attempted, the Speedwell technic being utilized. Its educational value was most important. The hospital's therapy should affect not only the child but the family as well.

The intern on pediatric service needs more training in the social problems of child and home. On a service of this kind the interns and resident physician for outpatients should follow patients into their homes.

To maintain its proper place in the health program the children's hospital must develop a more dynamic relationship to the homes from which its patients come.

DISCUSSION

DR. CLIFFORD G. GRULEE: Primarily a blank might protect the hospital against lawsuits. Whether it would have any standing in court I do not know, but I think that was the primary reason for the use of blanks.

Second, I should say that largely by chance we have had some sort of organization of this kind. There is an obstetric department for outpatients at Rush Medical College, and we have had an intern take care of new-born babies in the home. I think that it has developed a social consciousness in the minds of the interns that did not exist previous to that time, and I think that it is a good service. Interns are quite enthusiastic about it.

Another point is that possibly the situation might go still further than Dr. Schwartz has indicated. It seems to me that the hospitals of this country have in no way realized the possibilities. The hospital staff feels the responsibility for taking care of the children in the hospital, but no responsibility for children outside of the hospital. If the hospital were functioning for the care of the well as well as for that of the sick, then the child would be taken care of very well, the hospital serving both as a protective and as a curative institution, and it is possible that by doing this the number of charity patients entering the hospital would be reduced. At least 95 per cent of the children who go to hospitals pay practically nothing for the services they receive, and even in large hospitals it is unusual to have 5 per cent paying patients among the children.

DR. HENRY E. IRISH: I think that there should be a sharp differentiation between the cross-infections in hospitals as to wards and private rooms. All that has been said refers with truth to patients in wards. For a long time it has been quite evident that there is nothing more homicidal than children's wards. Every one knows that and knows all of the things that have been done to prevent epidemics. At Cook County Hospital it is our constant study to cut down the occurrence of cross-infections. I can subscribe to everything Dr. Schwartz stated as to the morbidity and mortality, but I think that we should differentiate sharply between the facilities of private rooms and of wards for these children.

DR. GEORGE E. BAXTER: I am impressed with the educational part of the program which Dr. Schwartz has presented. My memory goes back to the days when the young physician worked in the office of the already practicing physician. In other words, Dr. Schwartz' paper emphasizes a weak link in the present medical educational method of young men and women. They do not have that opportunity for studying and becoming acquainted with the environment of the patients. They have the training in the hospital and everything that goes with it, but there is little opportunity in most institutions to acquire environmental knowledge of the patients. I think that this presentation shows what an advantage it is to the young man, either during his internship or after, to have the opportunity of practicing medicine with some one who already has a practice, but of course that is too much to expect under present economic conditions.

DR. A. B. SCHWARTZ: I hope that if there is one thought I leave behind, it will be the one Dr. Grulee and Dr. Baxter commented on, the educational value of the idea. It would identify intern, nurse, physician and all others who work in childrens' hospitals with a program that will relate itself to the child and its environment rather than to the child alone. Some one said that it would be a good idea if once a year we reviewed all of our cases with this one question in mind: "What effect has the thing we did for this child had on the family?" If we answer that question, we shall have done the child a greater service than we are now doing for the patients in our childrens' hospitals.

PHILADELPHIA PEDIATRIC SOCIETY, NEW ENGLAND PEDIATRIC SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

HARRY BAKWIN, M.D., *Secretary*

Combined Meeting, New York, Oct. 21, 1933

MARTHA WOLLSTEIN, M.D., *Chairman*

PART 1. LOSS OF HEAT BY VAPORIZATION AND RADIATION. DR. EUGENE F. DU BOIS, New York.

The main channels of loss of heat from the body are radiation, vaporization, conduction and convection. There is accurate information regarding the total loss of heat and the share borne by vaporization. Information regarding radiation is incomplete and knowledge of conduction and convection extremely fragmentary. Further studies are needed not only for the benefit of those interested in heating, ventilation and clothing but also for the clinician who is concerned with the problems of loss of heat and water balance. Charts were shown giving an idea of the total production and loss of heat in normal persons and in patients with fever. The percentage of heat lost by vaporization was discussed briefly.

PART 2. LOSS OF ENERGY FROM THE HUMAN BODY BY RADIATION. DR. JAMES HARDY, New York.

The character of the body as a radiator as compared with that of the sun and other luminous bodies and the part that the color of the skin plays in radiation were discussed. A new technic for the measurement of the radiation and temperature of the skin was described and compared with the usual measuring devices of this kind. Examples of the measurements of temperature and of radiation were given to illustrate the method.

A CONSIDERATION OF THE NEW PREPARATION OF DIPHTHERIA TOXOID. DR. WILLIAM H. PARK, Department of Health, New York.

Diphtheria toxin-antitoxin, while effective, has certain drawbacks. Diphtheria toxoid has recently been developed as an improved product. Until within the last year the product used has been a toxoid containing approximately 10 antigenic units or a similar toxoid containing alum in a concentration of from 0.2 to 0.5 per cent. Two doses of such a toxoid produced immunity in about 80 per cent of the children in the course of three months and in from 90 to 100 per cent in the course of six months. The value of the alum was that it caused the toxin to be somewhat less soluble. Last summer Dr. Havens, of the Alabama State Board of Health, tried using the precipitate which is formed when alum is added to the toxoid in the concentration of from 1.5 to 2.5 per cent. This precipitate gave surprisingly good results. The effect was more than double that of the toxoid in fluid form. When from 10 to 20 antigenic units of this precipitated toxoid is used,

a single dose produces immunity in from 80 to 90 per cent of the children at the end of six months. This preparation is coming into universal use in this country.

A Clinical Investigation of the Development of Caries in the Deciduous and Permanent Teeth. Dr. Alfred F. Hess, New York.

In no other field is there such a marked diversity of opinion as in that of the etiology of dental caries. Even the question of the relative importance of systemic and local factors has not been satisfactorily decided. Recently deficiencies in the vitamins have been given a most important place in the field of etiology. Vitamin A, however, does not seem to be at fault if one can judge by the experience of Bloch, who found but little caries among the large number of children in whom vitamin deficiency developed in Copenhagen during and shortly after the war. Nor does the fault lie with vitamin B_1, judging from the experiences in the Far East where beriberi has failed to be associated with dental caries. Vitamin C, the antiscorbutic vitamin, is probably likewise not the essential factor lack of which is associated with caries. The very fact that dental caries is widespread in Florida, California and Hawaii and, on the other hand, is comparatively infrequent in Alaska and Greenland, where vitamin C forms a small part of the dietary, is important evidence in this regard. Vitamin D plays a part in the calcification of the teeth but a development of rickets does not primarily affect dental calcification. My associates and I have found that in our institution the children who had mild rickets during infancy had just as sound teeth when they were from 6 to 9 years of age as those who had been protected from rickets by treatment with cod liver oil or by other measures. This was true in regard to the permanent teeth; the incidence of caries among the deciduous teeth was somewhat higher for the rachitic group. This point of view is further fortified by the fact that the first molar tooth does not begin to calcify until the infant is 6 months of age, and the second molar tooth, not until the infant is nearly 4 years of age; in other words, after the rachitic period. Nevertheless, both of these teeth are markedly subject to caries. We found likewise that in a district in which rickets was almost all-prevailing some years ago the teeth of Negro children among a group of children from 8 to 14 years of age were sounder than those of a group of white children of similar age in the city of New York.

In studying the incidence of caries of the deciduous teeth among children during the first, second and third years of life in our institution for a period of ten years, we found definitely that the earlier the child was admitted to the institution the better were its teeth, in fact, that caries rarely developed in the teeth of infants admitted from under 6 up to 12 months of age. We attribute this superiority to the better dietary and to the use of various "calcifying agents" during the first and the second year of life. We believe that a calcifying agent should be given certainly throughout childhood and well up into adult life and, moreover, that the most satisfactory agent of this kind is irradiated milk which, at the same time, supplies the necessary calcium and phosphorus and functions automatically without the cooperation of the nurse or mother.

Some Clinical Aspects of Chronic Hemorrhagic Pachymeningitis. Dr. Rustin McIntosh, New York.

The type of hemorrhagic pachymeningitis which most concerns the pediatrician appears to arise spontaneously and, so far as can be ascertained, is not dependent on antecedent trauma, prematurity, nasopharyngeal or otic infection or congenital syphilis. In the majority of cases the first symptoms appear between the ages of 1 and 6 months, but the onset may be so insidious that nothing abnormal is noticed until much later. The essential process is the formation of a layer of fibrous tissue on the inner surface of the dura, within the meshes of which hemorrhages occur and cystlike cavities are formed. In the great majority of cases this fibrous tissue is widely distributed over the dura throughout the cranial cavity.

The common symptoms are convulsions, enlargement of the head, vomiting and attacks of crying. In general the symptoms depend on the extent and suddenness with which hemorrhage or exudation of serous fluid takes place. The diagnosis is suggested by a characteristic history and by the physical findings based on an uncompensated increase in intracranial pressure or by the presence of blood or xanthochromia in the spinal fluid. In some cases further confirmation is added by the detection of characteristic preretinal hemorrhages; in other instances, by the demonstration of a filling defect over the convexity of the brain by encephalography. Complete confirmation depends on aspiration of characteristic fluid from a cyst cavity by puncture of a fontanel.

The condition, formerly discovered only at autopsy, is now being more and more frequently recognized during life. In the past five years eighteen cases occurred in the Babies' Hospital: in 1928 four were recognized only at autopsy, none during life; in 1932 three were discovered clinically, and only one at autopsy. Puncture of a fontanel has therapeutic value in diminishing the intracranial pressure if the patient is in coma; otherwise it appears to have no therapeutic place, as the disease runs a spontaneous course. Of fourteen patients in whom the condition has been recognized clinically in the past nine years, five died while in the hospital, two have died since, four have serious and two questionable mental retardation, three have defective vision, and two show disproportionate enlargement of the head. Only two of these fourteen patients may be considered to have recovered completely.

EPIDEMIOLOGY REVIEWED IN THE LIGHT OF EXPERIMENT. DR. LESLIE T. WEBSTER, New York.

The background of epidemiology was outlined briefly, and some of the salient features of human epidemiology were mentioned. The epidemiology of human infections transmitted by vectors, animal hosts, water, food and fomites was traced in terms of fluctuating dosage and factors of resistance in the host. That of a small group of diseases transmitted by direct contact, in which the portal of entry is the upper respiratory tract, was considered as not yet interpretable. Experimental epidemiologic work on nine enteric and respiratory infections of rodents and fowl has consisted of observations on infections of population occurring spontaneously and induced experimentally, and measurements of virulence, dosage and resistance of the host during the actual spread of the infection. A technic has been evolved which is quantitative and yet produces the natural phenomena of infection. A major finding is that all the phenomena of infection thus far studied experimentally can be described completely in terms of factors affecting microbes and hosts. Another is that microbic virulence, although potentially variable, is relatively stable under natural conditions. A third is that microbic dosage varies with the amount and severity of infection, increasing prior to outbreaks, and decreasing prior to subsidence of infection. A fourth finding is that breeds and individual animals possess definite and varying amounts of inherited resistance to infection, that this resistance is affected by environmental factors such as season and diet and may be supplemented by immunity to infection. Finally, it was shown that the amount of resistance present in individual animals or in populations at a given time largely determines the extent and severity of the disease.

When these relationships are expressed in terms of cause and effect it appears that the severity of infections in these animal populations is regulated by stability of virulence and varying factors relating to dosage and resistance. In instances in which a foreign micro-organism gained access to a hitherto unexposed population, the inherent virulence, the available dosage and the amount and distribution of popular resistance together determined the extent and severity of the infection. In instances in which a micro-organism was already present in the population, variations in popular resistance and in available dosage were chiefly responsible for endemic and epidemic prevalences. Fluctuations in popular resistance were brought about by immigration, season and diet acting on the nonspecific components of

resistance and by the infecting agent stimulating the specific components. Fluctuations in available dosage resulted from variations in the resistance of the host and in factors affecting the vector.

To broaden the scope of experimental epidemiology the studies must be extended from the acute, highly fatal bacterial diseases of animals to the more chronic ones and to infections by virus. The last step is already being taken. Knowledge of many types of infection in many species of hosts will be required for the proper development of epidemiology as a science.

VIOSTEROL IN THE PROPHYLAXIS OF RICKETS IN PREMATURE INFANTS. LEONARD T. DAVIDSON, M.D., and KATHARINE K. MERRITT, M.D., New York.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

METABOLISM OF CREATINE IN MUSCULAR DISEASE. DR. A. T. MILHORAT, New York.

The abstract was not obtainable.

EFFECT OF TRAINING DURING INFANCY ON THE DEVELOPMENT OF BEHAVIOR (A STUDY OF TWINS). DR. MYRTLE B. MCGRAW, New York.

The purpose of the present investigation was threefold: (1) to ascertain when in the life of an infant it is reasonable to expect practice of particular functions to modify their course of development; (2) to determine whether daily exercise of primary reaction patterns such as the Moro reflex and the suspended grasping reflex weakens or strengthens their function during the later months of infancy; (3) to study the effect of irregularity of schedule, interrupted sleep and excessive stimulation on the general growth and well-being of an infant.

The subjects were twin boys. The weaker twin, selected as the experimental baby shortly after birth, was subjected to daily exercise (5 days a week) from the time he was 20 days of age. The larger twin was held as control. He was placed on a regular schedule which provided for a minimum of handling and social stimulation.

The records of growth of the two babies during the first year show remarkable similarities and equally remarkable differences. There is no indication that such traits as the Moro reflex, the suspended grasping reflex, sitting alone, erect locomotion, etc., can be appreciably modified by daily practice. On the other hand, certain other types of behavior can be greatly expanded through training. The experimental baby could, when less than a year old, crawl up an incline placed at an angle of 61 degrees, move about with equilibratory and locomotor control on roller skates, swim under water and make the initial movements toward diving into a pool.

Greater even than the differences in performance were the differences in attitude toward the experimental situations. The experimental twin was fearless and willing to attack any difficult situation, whereas the control twin was cautious and obviously insecure when placed in the same situation. He was more inclined to cry and to call on adults for help.

Although the study is incomplete, it does at the present time justify the conclusion that certain traits are subject to little modification through practice during the early months of infancy. Other types of behavior, particularly skills, can be greatly increased and improved by exercise. The effect of such training during the early months on subsequent development cannot be determined until future observations on the processes of growth of the subjects are available.

DISCUSSION

DR. CHARLES HERRMAN: If the twins had not been identical, it would have been necessary, in demonstrating that training had a favorable effect on behavior, to reverse the procedure and to see whether the more slowly developing twin would catch up with his brother. It is well known that fraternal twins may differ greatly in their development.

DR. M. B. MCGRAW: The only evidence that these twins originated from a single ovum is the single placenta. The preponderance of evidence is that they are fraternal twins. While the study would unquestionably be more impressive if the babies were identical twins, the fact that they are not does not, it seems, invalidate these findings. Especially is this so since the experimental baby has not only his twin brother but all other babies of corresponding age as controls. In some respects his performance exceeds that of any baby on record. This study is offered not as conclusive evidence in support of any particular theory but merely for what it is worth at this preliminary stage of the investigation. The experimenters are well aware of the limitations imposed by a study of so few subjects.

WATER REQUIREMENTS IN INFANTS. DR. S. Z. LEVINE, New York.

This report is concerned with the rôle of water in the bodily economy of infants as obtained through accurate studies of water balance in twenty-nine normal and dehydrated infants for a total of seventy-two days. Sources of available water and the pathways of the elimination of water, as well as a description of the procedures for obtaining the various increments, are considered. A study of the exchange of water in normal infants on varying intakes of fluid indicates that the physiologic mechanisms in the regulation of water are controlled primarily through the urinary output. An increased intake of fluid is reflected in a corresponding increase in the urinary output, so that normal infants do not retain appreciably more water in their bodies on high (425 Gm. per kilogram of body weight) than on low but presumably adequate (150 Gm. per kilogram) intakes of fluid.

Whereas the fecal water is a relatively trivial part of the total amount of water eliminated by normal infants, loss of water by way of the intestinal tract in infants with diarrhea is considerable, sometimes attaining alarming proportions. In one instance, an infant was able daily to excrete an amount of fecal water equivalent to one fifth of his total body weight. These amazingly high losses by way of the intestinal tract readily explain the tendency of infants with diarrhea to become and remain dehydrated.

In observations on infants preceding, during and following the induction of fever the rôle of the loss of water through the skin and lungs in the regulation of the heat of the body was demonstrated. This quota invariably declined during the rise in temperature and consistently rose during the fall. The results suggest that the compartment of urinary water is by far the most labile of all avenues for the elimination of water and that in a normal state of health this quota functions mainly in the defensive mechanisms of the regulation of water. Conversely, in febrile states, the relative constancy of the insensible water noted under ordinary conditions is affected, indicating that this quota functions mainly in the defensive mechanisms of the regulation of heat.

Studies of the exchange of water in infants, which have hitherto been relatively neglected, offer a new approach to the solution of many unsettled physiologic problems and many unexplained clinical phenomena.

BASAL METABOLISM IN CHILDREN WITH SPLENOMEGALY. DR. ANNE TOPPER, New York.

The basal metabolism was studied in thirty-three children with splenomegaly from various causes and in children in similar conditions but with apparently normal spleens, as controls. The subjects fall into four groups: (1) those with blood dyscrasias, (*a*) children with splenomegaly and (*b*) children with normal spleens;

(2) those with diseases characterized by icterus, (*a*) children with splenomegaly and (*b*) children with normal spleens; (3) those with malignant disease, (*a*) children with splenomegaly and (*b*) children with normal spleens; (4) those with splenomegaly of infectious origin.

The blood dyscrasias are a group of diseases in which there may be increased metabolism without recognized disturbance in thyroid function. The various explanations suggested for the increase in metabolic rate are: (1) the increased utilization of oxygen by the extra leukocytes; (2) the increased number of immature cells; (3) the severity of the anemia; (4) the increased excretion of uric acid.

The literature is filled with conflicting studies, those disproving all these theories as convincing as those proving them. Evidently some other explanation for the increased metabolism is necessary.

In the group reported on here, there was no constant relation between any of these factors and the basal metabolic rate. The only factor which seemed to parallel the metabolism was the splenomegaly. In the patients with enlarged spleens the basal metabolic rate was increased; in those with apparently normal-sized spleens the metabolism was normal. This apparent association between an enlargement of the spleen and an increase in the metabolism seemed to exist also in the other three groups.

Three questions arose and were discussed. 1. Is this association accidental? 2. Is there some other factor, toxic or hemolytic, at present unknown, which may be responsible for both the splenomegaly and the increased metabolism? 3. Is there a causal relationship between the diseased spleen and the disturbed basal metabolism?

Book Reviews

Die Behandlung der Kinderkrankheiten mit Ultraviolette- und Röntgenstrahlen. By Prof. Dr. W. Birk and Dr. L. Schall. Price, 12 marks, unbound; 14.40 marks, bound. Pp. 256, with 45 illustrations. Berlin: Urban & Schwarzenberg, 1932.

This book takes up in a very comprehensive way the various diseases of children in which ultraviolet rays or roentgen rays are advocated as a treatment.

The book is divided into two parts; the first deals with ultraviolet rays, the second with roentgen rays. Under each part the various methods of production and properties of the ultraviolet rays and roentgen rays are outlined, and the method of measuring the dosage is given. Also, the harmful effects that may complicate this form of therapy are dealt with in full.

Under each division the various diseases discussed are described and classified, and the methods of treatment are outlined. If indicated, the exact procedure, dosage and dangers of ultraviolet and roentgen irradiation are stated. Numerous cases illustrate the above points.

As befitting their importance, the subjects of rickets, tuberculosis and leukemia are dealt with in great detail. Other diseases dealt with under the division on ultraviolet rays are spasmophilia, infected wounds, whooping cough, asthma and similar conditions. Those discussed under the division on roentgen rays include Hodgkin's disease; malignant tumors; diseases with increased bleeding time; hemophilia; diseases of the central nervous system; brain tumors; hydrocephalus; feeblemindedness; postencephalitis; epilepsy; diseases of the glands of internal secretion—the thymus, pituitary, thyroid, parathyroid and suprarenals; pyloric spasm; inflammation of the lymphatic tissue of the throat, including the tonsils; bronchial asthma; bronchial pneumonia; acute inflammation; boils; phlegmons; infected glands; abscesses of the breast, and hemangiomas.

The book is concise yet complete in every detail and is an excellent reference in regard to ultraviolet and roentgen therapy.

The Science of Radiology. Edited by Otto Glasser. By twenty-five contributors. Price, $4.50. Pp. 450, with 108 illustrations. Springfield, Ill.: Charles C. Thomas, Publisher, 1933.

This book was written for "A Century of Progress" as a memorial volume, commemorating the pioneers in roentgenology and the advancement that has taken place in the youngest division of the medical sciences.

The book consists of a series of short articles by different authors, who present their material in a concise, authoritative manner and at the same time in the style of an interesting story.

A biography of William Conrad Roentgen and of Pierre and Marie Curie tells of their discovery of x-rays and radium, respectively, and the work of the American pioneers in roentgenology is recorded. Subsequent chapters outline the earliest knowledge concerning these rays, as contrasted with what is known at present, including the physics, apparatus, diagnostic and therapeutic uses, dosimetry, protective devices and hereditary and biologic effects of x-rays and radium. The progress in the military, cinematographic and industrial use of x-rays is briefly described.

There are a surprisingly comprehensive review of the literature dealing with roentgen diagnosis and an outline of the development of the teaching of roentgenology in the medical schools of America. The nature of the cosmic rays and the nitrogenetic rays (Gurvitsch) are described. Following each of the chapters is a good bibliography; that for the chapter on the literature on roentgen diagnosis covers eighteen pages.

The book is interesting and authoritative and will be useful as a reference book for any who are interested in the history or present status of roentgenology.

Le métabolisme et le rôle du facteur de croissance ou facteur "A" dans l'espèce animale et dans l'espèce humaine. By André Busson. Price, 30 francs. Pp. 182, with 15 illustrations. Paris: Gaston Doin, 1933.

In this monograph Busson reports the results of his extensive studies of vitamin A in animals and in man. The biologic, colorimetric and spectroscopic methods of analysis for determining vitamin A were carefully compared, and the results showed the biologic method to be much the most reliable. Experiments with carotene demonstrated that its rôle was apparently the same as that of vitamin A of animals. Many of the common vegetables and fruits were analyzed biologically for carotene, and the results are presented in tables. Analysis of the internal organs of animals and man showed that the liver was the chief depot for the storage of vitamin A and the regulator of vitamin A metabolism.

The use of the term "anti-infectious vitamin" is considered objectionable, since infection occurs only after the tissues have suffered great decrease in vitality and morphologic changes due to vitamin A deficiency. The "growth factor" is suggested as a much more appropriate designation.

The livers of new-born infants were found to be very low in vitamin A, whereas the livers of older infants and of adults contained appreciable reserves. The importance of maintaining an adequate intake of vitamin A in prolonged illnesses in the new-born is discussed. Various kinds of milk were analyzed for vitamin A potency.

The outstanding contribution in this study is the analysis of the livers of both children and adults in health and in disease. A great deal of material is available for practical clinical application.

Idleness and the Health of a Neighborhood. Issued by the New York Association for Improving the Condition of the Poor. By Gwendolyn Hughes Berry. Price, $1. Pp. 93, with 38 charts and 17 tables. New York: De Pamphilis Press, Inc., 1933.

This social study of the Mulberry Street district of New York City was undertaken to determine the extent of unemployment and its effect on the health of families, as compared with the health of families still having at least enough employment to maintain a standard of living above the subsistence level. This report offers definite information with regard to what actually happens to families in which unemployment is a serious factor. It is based chiefly on surveys made in November, 1930, and April, 1932, with some references to a survey of April, 1922.

The Mulberry Street district is composed almost exclusively of Italians living in tenements. The results of these observations substantiate the hypothesis that when people have no work their health suffers, as compared with families who continue to have work. In November, 1930, two out of five families reported all workers employed as usual, while in April, 1932, only one in five reported all workers employed. A great deal more illness of every kind was reported in 1932 than in 1930. The persons who were most frequently found to be ill were those from families with the poorest employment record, except for preschool children, in which instances no correlation between illness and unemployment could be demonstrated. The results of the survey are presented in detail with numerous tables and charts.

Die Erkrankungen der oberen Luft- und Speisewege des Kindes. By Max Meyer. Price, 10.80 marks. Pp. 184, with illustrations. Berlin: S. Karger, 1933.

This is the second volume of Professor Meyer's treatise on diseases of the ear, nose and throat in children. He modestly calls it a booklet, although it comprises 184 pages. As in his first volume, the author has again been led by the principle of being an adviser, on the basis of his own experience, to the house and children's

physician in his daily practice. But while in his first volume he treated the pathologic anatomy exhaustively, in his second volume he emphasizes the physiology, as he takes it for granted that the elements of the diseases in question are well known to every physician from courses in pathologic anatomy. Thus, too, he dwells less exhaustively on the diseases which are in practice almost always treated by the house physician. But again, as in his first volume, he marks the border between the realm of the house physician, on the one hand, and that of the specialist in diseases of the ear and throat, on the other. The illustrations have been masterfully drawn by W. Freytag and contribute to the practical and scientific understanding of the book.

The author dedicates this volume to the memory of his father, the late Dr. Edmund Meyer, Professor of Medicine in the University of Berlin and specialist in rhinolaryngology.

Hygiène scolaire. By L. Dufestal. Price, 50 francs. Pp. 438, with 129 illustrations. Paris: Gaston Doin & Cie, 1933.

The author is general secretary of the Society of Medical Inspectors of the Schools of Paris and of the Department of the Seine and also served as general secretary of the Third International Congress of School Hygiene. He speaks with authority and enthusiasm of the problems pertinent to his chosen field, and any one with similar interests will find his book a source of valuable information and stimulation.

The book is divided into five parts. The first is devoted to the construction of the school and its equipment. The best methods of lighting, heating and ventilation are discussed. Particular attention is paid to the classroom, the position of the windows and the type of desk and seat. The latter should be adjustable to the physical requirements of the pupils. The second part is concerned with the physical, intellectual and moral development of the pupil and points out the great harm that has been done by neglecting his physical well-being. The problems of fatigue and overcrowding of the school program are gone into. The third part emphasizes the importance of early diagnosis of disease and the need for prophylaxis in the control of contagious diseases. The fourth part is concerned with the activities necessary to assure as nearly as possible an equal opportunity to the child handicapped by poverty or physical defect. The fifth part has to do with the duties and opportunities of the school physician.

Enfance et hérédité. By A. Lesage. Price, 20 francs. Pp. 104, with 15 figures. Paris: Masson & Cie, 1933.

The general subject of diatheses in infancy and childhood is discussed. The rôle of inheritance in determining the constitution, predisposition and behavior of the child is considered to be of prime importance. Lesage believes that considerable information concerning the diathesis of the infant may be obtained from the cranial development and weight curve, even during the period immediately following birth. An original and simple classification of hereditary conditions consists of five divisions: (1) local inheritance, in which anomalies or morbid processes affect one organ or one system of the body; (2) inheritance of an infection, such as syphilis or tuberculosis; (3) inheritance of intoxication by alcohol, morphine, lead or other poison; (4) "explosive" inheritance, in which certain illnesses strike suddenly during later life, and (5) inheritance of arthritis.

The arthritic diathesis is discussed in detail with a consideration of the symptoms, general clinical course and treatment. The author speaks of the "ribbon which unrolls," bringing seborrhea and eczema in early infancy; asthma in later infancy; obesity in adolescence; migraine, hemorrhoids, renal and gallbladder colic, gout and diabetes in adult life, and chronic rheumatism in old age.

He states that this work is neither an erudite study nor a compilation, but represents a long series of observations and personal reflections.

Clinical Diagnosis: Physical and Differential. By Newton S. Stern. Price, $3.50. Pp. 364. New York: The Macmillan Company, 1933.

This book is a concise but comprehensive text for medical students and a guide for physicians. The subject is well covered, and the book gives a clear understanding of modern methods of clinical diagnosis. The material is well organized and without repetitions. The chapter on the taking of histories covers completely and compactly the matter of obtaining a satisfactory record of the patient's complaints. The methods used in physical examination are described in detail, and an outline for a logical procedure is given. Tuberculosis and heart disease are discussed at length, and the student is given an opportunity to become familiar with the majority of the findings in the chest.

In the teaching of differential diagnosis, the plan advocated by the author offers students a method of attack as well as a more intimate knowledge of disease processes. The many pages devoted to the signs and symptoms of various conditions are of the utmost importance.

The information contained in this book will give the student a better background and will serve the practicing physician usefully for reference.

La durée de la grossesse et ses anomalies. By Henri Vignes. Price, 15 francs. Pp. 96. Paris: Masson & Cie, 1933.

In this short monograph the author discusses the duration of normal pregnancy, with some remarks on prematurity and postmaturity. He shows that it is impossible to predict exactly when delivery will occur, because many of the fundamental processes concerned in pregnancy are not known. Three principal questions are considered in detail: When does pregnancy begin? What causes the onset of labor? What signs warrant the physician's being certain that an infant was born at full term?

None of these questions can at present be answered completely. Many case histories are presented to illustrate instances in which pregnancy was terminated much sooner or much later than was expected from calculation by the usual methods. The medicolegal aspects of this subject are briefly mentioned. Since the factors influencing the length of pregnancy are so numerous and so little understood, the author advises caution in predicting the date of delivery.

Zur Pathogenese, Klinik und Systematik der frühkindlichen Lungenentzündungen, in Beihefte zu Jahrbuch für Kinderheilkunde, Heft 32. By Dr. Alfred Wiskott. Price, 12 marks. Pp. 163, with 55 illustrations. Berlin: S. Karger, 1932.

This carefully prepared review by Wiskott includes 297 cases of pneumonia in early life, collected over a period of five years, and completely investigated clinically, pathologically and roentgenologically. The material was studied at the University Children's Clinic at Munich.

In the introduction, the various classifications of pneumonia and the recent work of Lauche, Nassau and L. F. Meyer are reviewed. The author divides the pneumonias of early childhood into three groups. The first he terms the "primitive forms." In this group he discusses the peribronchial type and the miliary type. Under the second subhead, the pneumonias of a "maturer type" are considered. His final division includes "mature" pneumonias. Here he discusses the early croupous type. A chapter is devoted to the influence of maternal immune bodies on neonatal pneumonia and the pneumonias occurring within the first three months of life.

This little pamphlet is well illustrated, containing roentgenograms, charts and diagrams; a full bibliography is appended.

Photochemical Immunization. By S. Peskind. Pp. 69. Cleveland: S. P. Mount Printing Company, 1933.

Photochemical immunization is the name chosen by Peskind to designate the procedure in which foci of infection are irradiated with ultraviolet light. It is claimed that this method is really a form of specific autogenous vaccination, since irradiation of a focus of infection causes the release of antigen from the focus, producing local as well as systemic immunity. Excellent results were obtained in more than one thousand five hundred cases of focal infection. The author explains the theory in detail.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Cleveland. Time: June 11-15, 1934.

American Academy of Pediatrics

President: Dr. John Ruhrāh, 11 E. Chase St., Baltimore.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Cleveland. Time: June 11-12, 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st. St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: Philadelphia. Time: Sept. 24-28, 1934.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May 3-5, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Kingston, Ontario. Time: June, 1934.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 Second Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245 Third St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, Tulane University, New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Battle Creek. Time: September, 1934.

Mississippi State Pediatric Society

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 16th St., Tulsa.

South Carolina Pediatric Society

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

Tennessee State Pediatric Society

President: Dr. Owen H. Wilson, 706 Church St., Nashville.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Chattanooga. Time: April, 1934.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: October, 1934.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. John A. Johnston, 2799 W. Grand Blvd., Detroit.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Muse, 384 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little, Jr., 817 Holman Ave., Houston, Texas.
Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Memphis Pediatric Society

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. T. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Secretary: Dr. John H. Reynolds, 1628 Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. James L. Gamble, 33 Edgehill Road, Brookline, Mass.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.

Philadelphia Pediatric Society

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. W. A. McGee, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Secretary: Dr. Ralph Verploeg, 19th and Gilpin Sts., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Armin C. Rembe, 1215 4th Ave., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. John F. Sanders, 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.

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